THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

MARCH, 1905.

A REVIEW OF ONE THOUSAND OPERATIONS FOR GALLSTONE DISEASE, WITH SPECIAL REFERENCE TO THE MORTALITY.[1]

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From June 24, 1891, to December 1, 1904, we had made 1000 operations upon the gall-bladder and bile passages, with 50 deaths (5 per cent.). About 95 per cent. of the cases were operated upon in St. Mary's Hospital and under nearly identical conditions.

In a rapidly growing field of this character there have necessarily been many changes in technique. For such improvements we are much indebted to the literature of the subject. We have benefited from the work of Murphy, Ochsner, Elliot, Richardson, Park, Bevan, McBurney, Halsted, and a host of others, and especially to the late W. E. B. Davis. To Robson, Moynihan, Kehr and Reidel, we wish also to acknowledge a debt of gratitude.

A study of mortality must be based upon some definite plan, and, so far as the writers know, there is no settled method upon which a correct estimate of the death rate in any series of operations can be compiled. What are we to understand by a mortality of a certain percentage? Some operators say that if a patient dies as a result of the operation itself, it should be counted; whereas, if the operation failed and the patient continued along for a time, then died from the disease or of a complication, it should not be charged to the operation. The defect in this method is that it allows of a large degree of personal equation, and the same statistics may be made to look very

[1] Read at the meeting of the Southern Surgical and Gynecological Association, by Charles H. Mayo, M.D., 1904.

well or very badly, as the critic is prejudiced for or against the operation. One very prominent operator declares that any individual dying within fourteen days from any cause should be attributed to the operation, and after that time it was a question to be settled by the judgment of the surgeon. In this series of cases we have taken the view of the layman, that if the patient goes into the hospital alive and comes out dead, the death resulted from (or in spite of) the operation. It is to be understood, therefore, that in estimating the death rate we have charged as a death from operation every patient who died in the hospital, without regard to cause of death or the time which elapsed between the operation and the fatal issue. It includes patients dying as long as three months after operation and from intercurrent disease or accidental cause, such as apoplexy, pneumonia, heart disease, chronic nephritis, etc. A percentage of the deaths could be fairly excluded, but as the object is to show the relative curability of gallstone disease rather than good statistics, we have concluded that the above method is at least unprejudiced. It undoubtedly has a tendency to exaggerate the dangers of operation, particularly in common-duct disease, where long-continued infections of the bile passages have resulted in blood changes, causing death at a late period. But it also illustrates the dangers of delay and the tendency to produce complications which operation may be unable to relieve.

In the 1000 operations there were 50 deaths in the hospital, or an average death rate of 5 per cent. In the benign series there were 960 cases with 4.27 per cent. For malignant disease, 9 deaths in 40 operations gives a mortality slightly in excess of 22 per cent.

Where the disease was limited to the gall-bladder, including all non-perforating infections, the mortality was 2.44 per cent.; 573 cholecystostomies, mortality 2.46 per cent.; 186 cholecystectomies, mortality 4.3 per cent. This does not include 101 cholecystostomies and 44 cholecystectomies performed as part of a common-duct operation. We have followed the rule of counting as one operation all the different procedures done through a single incision. The major or most serious is classified; the others are considered secondary and appear only in the record of the patient.

Of the common-duct operations there were 137 benign, with 16 deaths, 11.7 per cent. This gives a heavy mortality, but, as already pointed out, it is really a death rate of operation and disease, and means that 7 per cent. failed to recover from the direct results of the operation, that is, died within a few days; while 4 per cent. recovered from the operation, but did not regain sufficient strength to leave the hospital. Many cases operated were in desperate condition from prolonged icterus, anæmia, etc. No cases were refused operation if they so elected after a fair statement of the facts. Operations for malignant disease are discouraging; 40 operations, with 9 deaths in the hospital, and of those that recovered comparatively few received

sufficient palliation to repay the immediate risk, suffering, and expense. Two cases, however, can be considered favorable as to cure; both were instances of early carcinoma of the gall-bladder. In a few patients a thick-walled and functionally useless gall-bladder was removed, and examination showed malignant involvement, and in the 2 cases referred to no return has as yet taken place after more than two years. We have recently had 2 cases of a like character, but as yet too early to be considered as to the probability of cure.

Next to malignancy and acute perforative infections of the gall-bladder and pancreas, the most serious thing that can happen in gallstone disease is involvement of the common duct of the liver.

Contrast a mortality of 2.44 per cent. in 820 cases where the disease was confined to the gall-bladder with 11.7 per cent. in 137 cases where the common duct is involved.

It would exceed the limits of this paper to go into the details as to various operations performed, and we will confine ourselves to a short discussion of the mortality in the benign group of cases and a comparison of results after the three most common operative procedures, cholecystostomy, cholecystectomy, and choledocotomy.

It can be fairly stated that the average mortality of operations for diseases confined to the gall-bladder is not greater than for appendicitis in patients of the same age and condition of health. Gallstone disease is most frequent in people of advanced years—often obese and not infrequently the victim of some degenerative lesion of vital organs. One cannot directly contrast such cases with disease of the appendix, which is by far more common in younger and more robust subjects.

Cholecystostomy. Of these there were 573 (exclusive of 101 in connection with common-duct operations), with 14 deaths, a mortality of 2.46 per cent. This includes most of the acute infections with localized peritonitis. At least one-third of these deaths were from purely accidental causes that had to do with the general condition of the patient. The mortality of cholecystostomy in simple gallstone disease in otherwise normal individuals was less than 1 per cent. In 186 cholecystectomies (exclusive of 36 common-duct cases) the mortality was 4.30 per cent., or nearly twice that of cholecystostomies. It may be urged that this latter operation was elected in the more severe cases, and to a certain extent this is true, but not wholly so, as the more dangerous acute infections were nearly always drained by cholecystostomy. Inasmuch as in not a single instance did stones reform in the gall-bladder when left, cholecystostomy must be considered the safe operation, cholecystectomy being reserved for certain cases in which cholecystostomy may be expected to furnish, in a considerable proportion of cases, a partial or complete failure. Other things being equal, all cystic gall-bladders should be removed, and especially when a stone is impacted in the cystic duct, as not infrequently a stricture may follow removal, interfering with the

escape into the common duct of the normal secretions of the mucous membrane, thus giving rise to colics or external mucous fistula. As a rule, gall-bladders which are found to contain bile at the time of operation may be drained, as if bile can get through the cystic duct mucous secretion can escape. If the cystic duct should be considerably injured during removal of the calculus, introducing doubt as to the future permeability, the gall-bladder should, of course, be removed. Again, gall-bladders which are suspiciously thick and hard should be excised, as in this way early malignancy may occasionally be cured, as shown in the 2 cases referred to above.

In most cases of chronic cholecystitis without stones the gall-bladder should be removed. The presence of gallstones gives rise to irritation, and their removal, with subsequent drainage by cholecystostomy, may be expected to leave a harmless organ, but an infection which is able to continue without the aid of foreign bodies calls for a more radical operation.

We must not be too ready to diagnosticate cholecystitis without stones on operation, or we may cover a mistake in diagnosis, and send home an unrelieved patient with an unnecessary operation. Before a diagnosis of non-calculous cholecystitis is permissible, the duodenum, stomach, pancreas, appendix, and right kidney must be examined, and if the theory is correct the gall-bladder should be found thickened, of light color, with the lymphatic glands along the cystic and common ducts markedly enlarged. It should contain tarry bile and the mucous membrane should be not only thickened, but covered with little, fibrinous specks.

In patients who have gallstones and who have suffered from attacks of jaundice and other symptoms of infection of the common and liver ducts, but without stones in the ducts, cholecystostomy is the operation of choice, as it furnishes bile drainage. Cholecystectomy, if performed in this latter group, should not be accomplished by ligating the cystic duct, as it may be vital to secure bile drainage, and the duct must be left open, or, if necessary, split down to the common duct for this purpose. If the cystic duct is patulous, cholecystostomy furnishes this drainage easily and safely, and in case of future common-duct stone, the gall-bladder is a reliable guide to the common duct and greatly facilitates a secondary procedure.

It must be borne in mind that stones may form in the common duct secondary to an infection from gallstones in the gall-bladder, and especially so if a stone has passed through the common duct or has been removed from it. It has been urged that the gall-bladder in gallstone disease is obsolete and should be removed in every case. In our experience there has been a slightly increased hazard and without compensating increase in permanence of cure or shortening of convalescence in the average case. We find indication for removal of the gall-bladder in about 2 cases out of 5, but consider cholecystostomy the operation of choice, and only perform cholecystectomy

for definite pathological conditions, such as we have called attention to.

The most common cause of death where the gall-bladder alone was involved has been a descending infection of the common and hepatic ducts. Cholangitis, as a result of gallstone disease, at once introduces a most serious complication. As long as the stones were confined to the gall-bladder they were, so to speak, but a side issue to the possibilities of trouble engendered by lodgement in the deep ducts, for here an infection is lighted up which may extend to the smallest bile ducts, and over which, as compared with gall-bladder disease, we have but little control. A process is instituted which may result in stone formation, even in the most minute bile ducts, and future trouble after apparent cure may be the result. The death of 16 patients in 137 operations for gallstones in the common-duct series and 4 out of 9 malignant cases at once demonstrates the serious character of common-duct surgery. Not that the operation itself is particularly difficult nor prolonged, but we have two serious elements introduced, jaundice and infection, and the mortality, both immediate and remote, of choledochotomy depends almost entirely upon these factors. About one-third of all patients with common-duct stones have little or no jaundice at the time of operation and very little infection. However, at the time the stones passed into the common duct there will usually be found in the history that there had been both jaundice and infection, and during the acute stage operation would have been fraught with greater danger. During the quiescent period operation is very safe in such patients, and the mortality in our experience not more than 2 per cent.

Unfortunately, the majority of common-duct patients have either never had an intermission or have passed beyond it, and operation is no longer an election as to time, but a necessity, and, no matter how desperate, must be done to save life. In some cases the infection is the more prominent feature, giving typical ague symptoms. Sudden chills, with high temperature, followed by rapid decline, and a little temporary increase in jaundice and attended with moderate pain, and often nausea, are pathognomonic. In others there is little infection, but such a degree of bile stasis in the ducts as to invite infection after any kind of operation. Some individuals are almost sure to die. Patients with extreme jaundice and subcutaneous hemorrhage will nearly always bleed to death from capillary oozing. If purpuric spots exist with jaundice, we keep the subjects under treatment until the blood will at least remain in the proper channels. In all cases of jaundice we use chloride of calcium, following the advice of Robson for a few days before operation, but we are uncertain as to its exact value.

Another class of cases who have in our experience all died, and about whom we are not always able to foretell the conditions previous to operation, are those patients with obstructive jaundice in

whom no trace of bile is to be found in the bile passages, the common and hepatic ducts being filled with clear fluid. The liver has been put out of action. The patient, while extremely feeble, may be up and about. The jaundice is extreme, but is not necessarily accompanied by leaky bloodvessels and subcutaneous hemorrhages. We have had 4 of these cases, and all died within four days. In 2 cases a little bile appeared in the drainage at the end of twenty-four hours, but in none did liver action become re-established.

In a number of instances the same condition was met with at an earlier stage, the bile ducts being filled with thick, flocculent bile of a dark-greenish color, very much like that which occurs in the gall-bladder during the acute stage of cystic-duct obstruction and before the pigments have become absorbed. In about half of this group the liver will begin to functionate and the patient recover. In reviewing the deaths in common-duct operations, one is impressed by the influence of jaundice, not only in vitiating the general health of the patient, as shown in the tendency to capillary bleeding, but even more important in the invitation which it extends to infection. Combined jaundice and infection is the cause of most of the late deaths from general debility and exhaustion which occur after a primarily successful operation. While we have had no cases in which stones have reformed in the gall-bladder after cholecystostomy, we have had 2 cases in which stones formed in the common duct, after the removal of a single large stone from the gall-bladder in 1 case and in the other many stones from both gall-bladder and common duct, showing that stone formation may take place independently of the gall- bladder, but only when there have been primary stones in this viscus.

We have seen a number of cases of liver-duct stones, but there has always been a blocking common-duct stone from the gall-bladder at the papilla behind which the intrahepatic calculi had formed, the favorable condition of partial obstruction and mild infection furnishing the proper environment. In 2 cases we have had to operate a second time upon common-duct stones which had for their nucleus hepatic-duct stones which had drifted down into the common duct subsequent to the choledochotomy. In the 1000 operations, 14.6 per cent. involved the common duct.

THE PSEUDOMALARIAL TYPES OF INFECTIVE ENDOCARDITIS.[1]

By Warren Coleman, M.D.,
of New York City.

Cases of infective endocarditis simulating malarial fever have been reported from time to time for half a century, yet adequate recognition has scarcely been given to the subject in text-books. Nor has the attempt been made, so far as I am aware, to bring together the various types. The importance of infective endocarditis and the difficulty often encountered in arriving at a correct diagnosis apparently justify a consideration of the pseudomalarial forms under which it may be masked.

Before the discovery of the malarial parasite, especially, the attempt was made to establish an etiological relation between malarial fever and infective endocarditis. It was entirely *post hoc* reasoning. Convincing proof of such relationship has not yet been offered. In fact, it is almost universally conceded that anteeedent or coincident malaria is merely fortuitous. Some cases have given histories of recent or old-recurring malarial attacks, but these histories must be accepted with caution, at least in certain instances. The pseudomalarial types of endocarditis are subject to complete, though temporary, interruption for weeks at a time. Herzog has reported the coincident presence of the malarial parasite in one case, but does not prove its etiological significance. It was present also in a fatal case treated at Bellevue, and in another at City (Charity) Hospital.

The cases of infective endocarditis of pseudomalarial type which have been reported fall broadly into two groups, acute and chronic. The duration of the acute cases is measured by weeks, of the chronic by months. It will often be found, however, that cases which have died after a few weeks' observation give histories extending over several months. Other chronic cases may continue for eighteen months or more.

The pseudomalarial must be distinguished from the frankly septic and pyæmic forms of infective endocarditis, of which they constitute a remarkable sub-group. They differ rather in the periodicity than in the nature of the paroxysms. Their resemblance to malarial fever is often very exact. The paroxysms may recur at regular periods, even at the same hour, and the intervals be fever-free. In the apyrexial periods the temperature is often subnormal. No special infective agent is responsible for the pseudomalarial types, nor is it necessary that there shall have been previous cardiac valvular disease.

[1] Read before the Section on Medicine, New York Academy of Medicine, October 18, 1904.

The cause of the periodicity has not been determined. It has been thought to be due to disturbance of the heat-regulating mechanism by an antecedent malaria, and that the stamp of malaria is carried by the subsequent febrile movement. This seems unlikely, since no other febrile disease, when it follows a malarial attack, pursues such a course. Nor has it even been proved that the majority of cases have been recently preceded by malaria. Sicard found staphylococci in the blood in the pyrexial but not in the apyrexial periods of one case.

The following pseudomalarial types have been reported:

1. Double quotidian.
2. Quotidian.
3. Tertian.
4. Quartan.
5. Septan.
6. Mixed types.
7. Irregular.

A single case may present during its course several of these types, yet at a particular period each type be pure. It is almost characteristic of these cases that they change their course. In spite of this fact, it is advisable to speak of distinct types. Cases may be under observation for short periods only, during which a definite type is preserved.

When the disease is approaching a fatal termination, the paroxysms often return irregularly.

Characters of the Paroxysms. The paroxysms may be identical with those of malarial fever, presenting cold, hot, and sweating stages, with fever-free intervals. The cold stage may be accompanied by a prolonged, hard chill, or simply by sensations of chilliness. As in malaria, the temperature may rise steadily through the chill. The chills begin with or after the initial rise of temperature, which, though sharp, may occupy several hours in reaching its maximum. In acute cases the maximum is often very high, even 107°. The defervescence is sudden and generally marked. The temperature may fall 1° or 2° below normal. Subnormal interval temperatures have occurred in a number of cases. Sweating may be profuse, scanty, or absent. It is commonly present. Vomiting often accompanies a paroxysm. A single paroxysm may occupy from six to eight hours. The intervals between the paroxysms may be fever-free or show a slight febrile movement.

The Onset. The onset is often like a simple malarial attack. The type may be established at once, or only after a period of irregular paroxysms. When first seen the patient may give a history of recent apparent malaria, with apparent relief from quinine. Such a history almost necessarily deceives one at first as to the true nature of the illness. It has probably led also to the false assumption of recent malarial attacks by some authors.

1. Double Quotidian Type.—I have been able to find only one case in which this type was followed unchanged to the fatal termination. The double quotidian type has generally appeared only toward the end of the disease. The previous course may have been quotidian, tertian, or irregular.

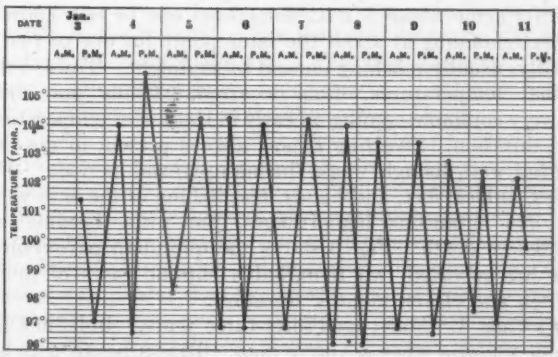
Illustrative Case. Coupland's Case I. Male, aged forty-one years. Gonorrhœa at twenty, otherwise healthy. Took cold two months ago. Next day had pain in left leg, which was relieved by local applications. Patient always felt weak afterward. Five weeks ago began to suffer from "shivering fits," from which he has not since been free. Paroxysms at irregular intervals, some every third day, some every fifteen hours. Thought he had ague. Each attack was accompanied by vomiting and was followed by an intolerable sense of heat. Became progressively weaker. No pain, but noticed latterly that legs swelled toward night.

Status Præsens. Looks very ill; is spare and sallow. Lungs practically normal. Cardiac dulness normal. Rough systolic bruit at apex. No thrill. Pulmonic second sound ringing; aortic dull.

Course. Throughout whole course, pyrexial periods averaged about five hours. Rigors, which sometimes commenced with and sometimes after the initial rise of temperature, averaged one and one-half hours' duration. The apyrexial periods, during which the temperature frequently fell to extreme subnormal levels, averaged ten hours. Absence of sweating was a marked feature.

Fig. 1 represents the double quotidian paroxysms. Fig. 2 represents double quotidian changing into quotidian paroxysms.

Fig. 1.

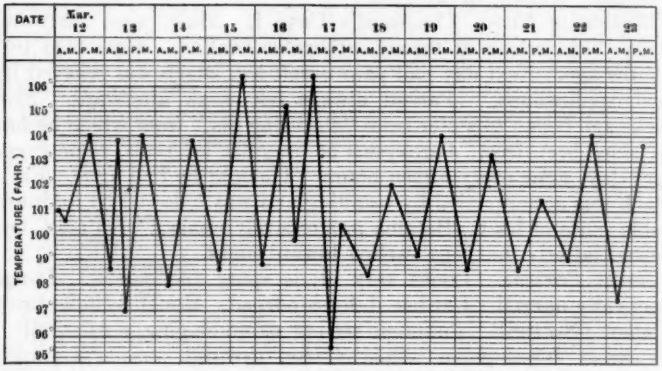


Double quotidian type. Coupland's Case I.

2. Quotidian Type. *Illustrative Cases.* Dock's Case I. (1895). Female, aged twenty-six years. Forceps delivery, with laceration

of perineum. Wound healed quickly. Three weeks later went sleighing. Afterward remained in bed. Had chills, fever, and sweating almost every day.

FIG. 2.



Double quotidian changing to quotidian. Coupland's Case II.

Status Præsens. Slight emaciation. Moderate effusion in right knee. Feet painful, but not swollen. Fugitive painful swellings in fingers. Heart enlarged, impulse heaving, loud mitral systolic murmur. Second sounds normal. No cardiac lesion found at examination prior to administration of chloroform for forceps delivery.

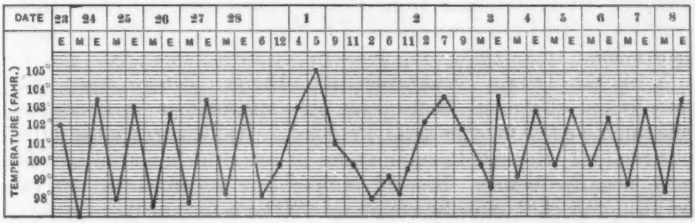
Course. Rise of temperature usually occurred about noon, reached its acme about 5 P.M., sometimes one or two hours later, and after remaining at about the same point for one or two hours fell rapidly, usually reaching normal by midnight. Toward the last subnormal temperatures often occurred. Chills not constant, though very common, coming on early in the rise of temperature and of short duration. Sweating almost always present in the decline. Patient felt well, though weak, during apyrexial periods. Pain in the knees, ankles, feet, and hands, and itching of the skin were frequent. No cutaneous hemorrhages, but urine became bloody shortly before death. Fig. 3 shows the quotidian paroxysms.

Osler has reported two remarkable chronic cases of quotidian type of ten and eleven months' duration.

Osler's Case I. Male, aged forty-three years. Indefinite history of chronic malaria when a young man. Illness began with a chill, followed by fever, malaise, and muscular soreness. Headache, loss of appetite, insomnia, and cough were marked symptoms. Spleen large. Symptoms abated in a few days and patient resumed business. Three weeks later marked dyspnœa, with increasing cough,

developed, and a loud systolic murmur was heard at the apex for the first time. Had daily intermittent fever, usually subnormal in the morning, and ranging from 102° to 103° in the evening, with occasional sweats. Pains in different parts of the body, particularly in the left inguinal region; tenderness over the fourth and fifth left costal cartilages. Fever continued throughout winter, with weakness, cough, and dyspnœa. Patient in the Johns Hopkins Hospital

FIG. 3.



Quotidian type. Dock's Case I. (1895). Portion of chart.

from March 15th to May 10th. There were no chills, only slightly chilly feelings. Morning temperature was 97.5° to 98°, with a gradual rise to 102° to 103° at 4 P.M., and a gradual fall to normal at midnight. Between 4 and 5 o'clock in the afternoon, sometimes not until evening, there was sweating, occasionally profuse; more frequently the skin was only slightly moist. The general condition improved somewhat, and the patient gained slightly in weight. The only complaint was pain in the splenic region, sometimes with very distinct tenderness. There was no change in the cardiac condition while in the hospital. The temperature range was low, and often subnormal toward the end. Petechiæ appeared. Sweating continued. The patient failed progressively. Diarrhœa developed. The urine contained blood and blood casts. Death.

3. TERTIAN TYPE. *Illustrative Case.* Elsner's Case I. Symptoms of intestinal infection for several days. At the same time had a persistent gonorrhœal discharge. Without marked disturbances of any kind, without evidences of constitutional infection, patient suddenly developed a tertian form of intermittent fever, and ague was suspected. It became evident after the third day that the prostration was greater than in malaria, the delirium more marked, and nervous symptoms more profound. There was increasing shortness of breath. Heart rapid, sounds suggestive of mitral insufficiency. Spleen large. Albuminuria. After the third chill, in spite of the fact that the tertian type of fever persisted, the temperature was always slightly elevated. Physical signs of auriculoventricular insufficiency, with aortic stenosis. Death in fourth week, in typhoid

condition, with hemiplegia, occasional chills, and sharp rises of temperature. Fig. 4 shows tertian paroxysms.

4. QUARTAN TYPE. *Illustrative Case.* Wenckelbach. Male, aged fifteen years. Entered eye clinic, after measles, for interstitial keratitis. Developed intermittent fever, complained of palpitation. Heart enlarged; sounds clear, but accentuated. Fever followed quartan type. Intervals not fever-free. No malarial parasites in blood. Daily attacks of palpitation, up to 160 per minute. Heart still further enlarged. Spleen enlarged, with piercing pains. Staphylococcus albus obtained from blood. Diagnosis, infective endocarditis. Cured after injections of collargol. Fig. 5 shows quartan paroxysms.

5. SEPTAN TYPE. *Illustrative Case.* Henry. Female, aged nineteen years. Typhoid three years ago, rheumatism in childhood, pneumonia a few months ago. Pregnant. Well-compensated mitral obstruction. Repeated examinations of blood for malarial parasite gave negative result. Rise of temperature accompanied on two occasions by chill, once by vomiting. "The inference that the fever is dependent on the heart lesion is based on the fact that no other cause could be found for it." Patient recovered.

This case is the only one of pure septan type that I have been able to find, though septan paroxysms have occasionally occurred toward the end of cases which at other times had followed other types. Fig. 6 shows the septan type.

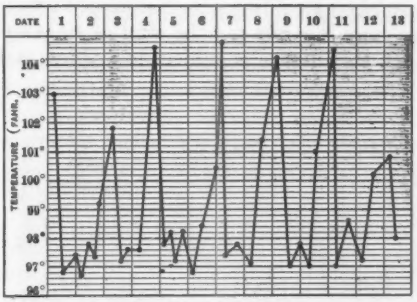
6. MIXED TYPES. These may be dismissed with a few words. The term is employed to designate only those cases which present two different types simultaneously. Such cases must be extremely rare. I have not been able to find even one which followed this course uninterruptedly. However, since Finlayson's case presented mixed tertian and quartan paroxysms during two months of its course, it seemed necessary to include the "mixed types." Fig. 7 is a part of the temperature chart of Finlayson's case.

7. IRREGULAR TYPES. The irregular types constitute by far the majority of cases of infective endocarditis which bear resemblance to malarial fever. The resemblance rather dates back to the time, however, when exact knowledge of the malarial parasite had not been acquired—when cases were diagnosticated as malarial fever simply because of recurring periods of pyrexia. No less an authority than Dreschfeld states, in Allbutt's *System of Medicine*, that all cases of chronic infective endocarditis resemble malarial fever. Such a statement is, to say the least, unfortunate.

The irregular acute cases are generally so clearly septic and the constitutional symptoms so marked that there is little difficulty in recognizing them, while the chronic cases are generally so irregular and so frequently develop in the course of chronic cardiac valvular disease that one is not left long in doubt as to their real nature.

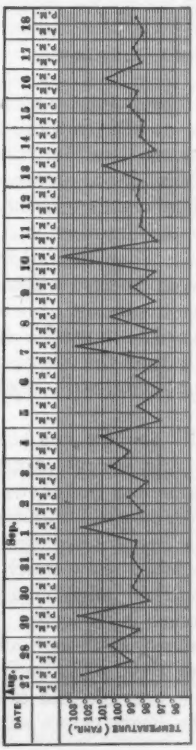
Diagnosis. The diagnosis of a pseudomalarial form of infective endocarditis is often very difficult. As in other varieties, the heart

FIG. 4.



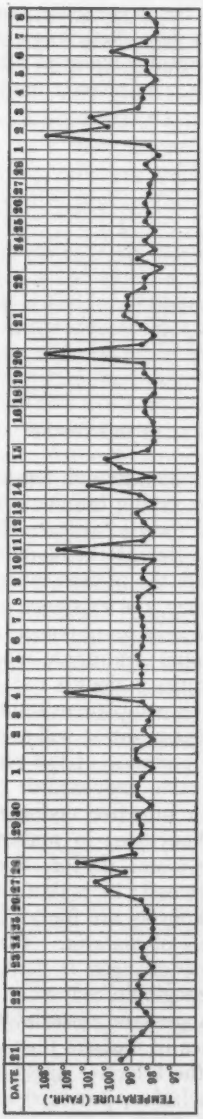
Tertian type. Portion of chart of Finlayson's case.

FIG 5.



Quartan type. Wenckelbach's case.

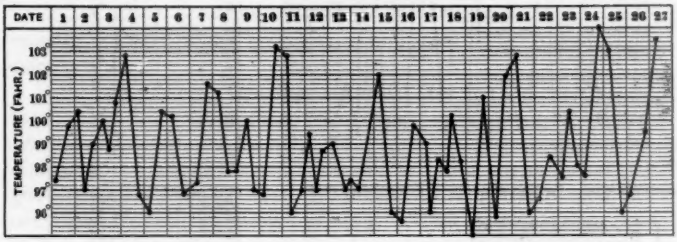
FIG. 6.



Septan type. Henry's case.

may give neither signs nor symptoms. If the infective process has been engrafted upon an old valvular lesion, the diagnosis need not present much difficulty, nor if an atrium of infection can be found. But the cryptogenic cases, occurring in persons previously healthy, or in those who, living in suspicious localities, give histories of recent apparently malarial attacks, may severely tax the skill of the clinician. As already mentioned, the disease is subject to sudden and

FIG. 7.



Mixed tertian and quartan types. Portion of chart of Finlayson's case.

complete, though temporary, interruptions. The patient may have been taking quinine. Under the circumstances, what is more natural than to assume that the quinine has stopped the paroxysms, even though the blood may not have shown the malarial organisms? When the patient returns for treatment, or if he comes with such a history, the existence of malarial infection is presumptive, and the case may go unrecognized, at least for a time. Then the failure of quinine to mitigate or arrest the paroxysms gives the first intimation that the patient is not suffering from malaria—assuming, of course, that a complete examination of the blood has not been made. Such an examination will at once rule out malaria, but, on the other hand, the presence of the malarial parasite does not necessarily exclude infective endocarditis (*vide* Herzog's case).

In infective endocarditis there is generally though not always leukocytosis; in malaria, leukopenia is the rule, except during a paroxysm. In infective endocarditis the polynuclear leukocytes are increased; in malaria there is relative lymphocytosis. Pigmented leukocytes are found in nearly all severe and protracted or fatal cases of malaria. The red cells and hæmoglobin show much the same changes in both conditions—rapid, marked oligocythæmia, hæmoglobin reduction, and degenerative changes in the cells. The changes are essentially those of secondary anæmia, though sometimes in malaria they pass into the pernicious type. The recovery of the infective agent from the blood is often possible and always conclusive, provided no other nidus than the heart valves can be found.

One of the remarkable features of these forms of infective endocarditis is the strength of the patient between the paroxysms. Until the disease is advanced he may feel quite well, and the classical picture of sepsis be lacking. Changes of type commonly occur during the course of the disease, and should be of much aid in diagnosis. In Ord's case, for example, the type changed from quotidian (two weeks) to tertian (two weeks), then to quartan, and later became irregular, the paroxysms recurring sometimes at intervals of a week. If an obstructive valvular lesion develops in a case pursuing a malarial course, the disease is almost certainly infective endocarditis. But, after all has been said, many cases will prove difficult to diagnosticate.

Pathological Anatomy. The simulation of malaria by infective endocarditis appears again in manycases in the pathological anatomy and histology of the viscera. In both diseases the long-continued hæmolysis results in the deposit of pigment in the spleen, liver, and bone-marrow, and while in malaria this pigmentation is much more extensive, owing to the activity of the parasites, nevertheless, the pigmentation of the viscera seen in septic processes often reaches a grade quite comparable to that of malaria. Thus, the spleen in septic processes may be considerably enlarged, distinctly brownish in color, and in very acute cases nearly diffluent. Likewise, the liver may exhibit a brownish or leaden color, much like that of malaria. Histologically, there is the same filling of endothelial cells of pulp and capillaries with masses of granular and globular pigment, the minute morphology of which is very similar in both malaria and infective endocarditis with bacteræmia. Hence it is unsafe to attempt to distinguish malaria from septic processes merely on the gross or microscopic appearance of pigment in the viscera. The only reliable method is the demonstration of the bodies of malarial parasites in cases of this disease, and their absence in septic processes. In nearly all other respects the pathological anatomy of pernicious malaria may be closely reproduced by septicæmia.

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DISSEMINATED SYPHILITIC ENCEPHALITIS.

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The following study is of a case of syphilis of the central nervous system, which presents points of interest in its pathological histology and as an example of the occurrence of severe syphilis of the nervous system soon after infection, at a time when the constitutional symptoms were still marked. There occur in the nervous system a variety of lesions, some of which may be regarded as specific; others cannot be differentiated from simple inflammatory phenomena. These inflammatory phenomena occur throughout the entire cortex, and also as focal areas of granulation tissue. These latter so overshadow the other features that it seems best to designate the case one of disseminated syphilitic encephalitis.

Summary of the Clinical History. C. C., male, aged forty-one years, admitted to the Danvers Insane Hospital, December 11, 1902. Family and early personal history not noteworthy. While not a steady drinker, he occasionally used alcohol to excess. June 12, 1902 he consulted a physician, giving a history of syphilitic infection three weeks previous, and then showed an initial lesion on the dorsum of the glans penis. On July 2, he was again seen by the same physician at a time when just recovering from an alcoholic debauch. The primary sore then showed extensive ulceration, and there was a papular eruption over the arms, chest, abdomen and legs. He was put upon a specific treatment of mercury, with occasional weeks of mixed treatment. An attack of iritis occurred, but soon disappeared with increased dosage. In the latter part of November, or about six months after infection, he had severe headaches which could be only partially controlled by treatment. Soon he became forgetful and was described as being "stupid." He was neglectful of his personal habits and "too stupid to eat." This condition led to his commitment to this hospital.

The examination made at his admission by Dr. Mitchell shows that he was poorly nourished, weighing 124 pounds. He was so

feeble that he was immediately put in bed. His face was dull and expressionless. He moved restlessly from side to side and made coarse purposeless movements with his arms. A general eruption was present; over the arms and legs this was of more or less discrete scaly papules, over the chest more of a maculopapular type. On the dorsum of the glans penis there was a recent scar. In the mouth were a number of mucous patches. The inguinal and epitrochlear glands were enlarged.

The left pupil was larger than the right. Light reactions could not be tested satisfactorily on account of the patient's restlessness. There was external strabismus of the right eye and partial ptosis of this lid. The knee-jerks were increased and there was a crossed adductor reflex. No ankle clonus. There was coarse tremor of the arms and hands. Tongue steady when protruded. Mentally, he showed extreme clouding of consciousness; only occasionally could his attention be gained and a relevant answer obtained to the question. Disorientation was complete. He was stuporous and frequently dozed during the examination.

December 15*th*. Stupor more marked; he showed coarse restlessness and moved purposelessly about the bed. He passed his urine and feces without control. His attention was obtained only by loud tones, and could not be held.

17*th*. Difficulty in swallowing, the food regurgitating through the nose. Ptosis of right lid more marked; slight external strabismus. Muscular twitchings of the right side.

18*th*. Comatose. Irritation of the left leg produced twitchings of the left leg and arm. Slight spasticity of right arm and leg. Left pupil larger than right; neither reacted to light stimuli. Died on this day.

Autopsy Five and a Half Hours Post-mortem. Male body, aged forty-one years, moderately well developed, but poorly nourished. Post-mortem rigidity is present only in the lower jaw. In the conjunctiva of the inner half of the left eyeball is a diffuse hemorrhage. Scattered over the thorax and abdomen are many yellow-brown scars; most of these measure a few millimetres in diameter, the largest rarely reaching 10 mm. On the arms are numerous papules with scaly tops. On the legs are many pigmented scars similar in appearance to those on the thorax; among these are scattered papules with scaly crusts; around the ankles are similar papules; the skin about these shows several small, scattered areas of ecchymoses.

Heart. Not notable save for a small hemorrhagic focus in the mitral valve.

Lungs. Considerable œdema and hypostasis in the posterior parts. In the left apex is a firm nodule 1 cm. in diameter.

Microscopic Examination. This nodule appears as a caseous substance surrounded by a thick fibrous capsule. Capillaries

throughout the section are intensely engorged. In some of the alveoli there are a few polynuclear leukocytes and epithelioid cells; many of these latter have inclusions of pigment granules; fewer have one or two red cells and occasionally a lymphocyte.

Spleen and Kidneys. Not notable.

Liver. Capsule of the left lobe shows a broad, milk-colored patch of thickening. Liver substance considerably engorged.

Microscopic Examination. Sections through the capsule show an increase of connective tissue with infiltration of lymphoid cells between the fibrils. The periportal connective tissue is much increased. Many of the central veins are engorged and the capillaries dilated. The liver cells of the central part of the alveoli frequently show fatty degeneration.

Sections through a papule of the skin of the arm show at one place an infiltration of the stratum corneum with polynuclear leukocytes, otherwise the epidermis is not notable. In the cutis there are places where accumulations of lymphoid and plasma cells and the fixed tissue cells are swollen. The bloodvessels here and in the subcutaneous areolar tissues have their walls crowded with plasma cells. The coil glands are strikingly free from cellular accumulations.

Sections through the glans penis show dense infiltration of the cutis with lymphoid and plasma cells among which are many mast cells. Focal accumulations of these cells lie deep in the tissue of the glans. The other internal organs show nothing unusual.

Cultures from the heart, spleen and meninges were negative.

Head. Calvarium and dura mater not notable. The pia mater of the convexity shows a slight haziness. Over the base, especially below the cisterna and from here spreading out over the pons and into the fissures of Sylvius on both sides, it is thickened, hazy, and hyperæmic. The thickening is most marked around the root of the right third nerve, and here the pia has a grayish, gelatinous appearance. The left middle cerebral artery, in the first part of its length, is considerably thickened.

The brain was sectioned after the method of Meynert, and in the gross showed nothing unusual except a small hemorrhage among the pyramidal fibres of the right side of the pons; here there is one hemorrhagic area about 7 mm. in diameter, around which are numerous small punctiform hemorrhages. The brain weighed 1360 grams. Save for a slight haziness of the pia, the cord showed nothing unusual in gross appearance.

At the autopsy some material for the following histological study was immediately fixed in Zenker's fluid and in alcohol. The remainder of the brain and cord were put into 10 per cent. formalin, and after a few days hardening the other material studied was cut and used for a variety of methods.

The descriptions of the meningitis are chiefly of material taken

from the frontal regions and from the pia at the base of the brain fixed in Zenker's fluid and stained with eosin and methylene blue.

That of the bloodvessels from similarly prepared sections.

The descriptions of cell changes of the cortex and cord are of alcohol-hardened material taken from the frontal, parietal and calcarine regions and various levels of the cord cut unimbedded and stained according to Nissl's method. Later further material was cut out from the formalin-hardened brain and put into alcohol and then stained in a similar way. The glia fibre studies are of material cut from the brain after a few days in 10 per cent. formalin and stained by Weigert's method; and of material cut the same as for Nissl's method but stained according to Benda's method for neuroglia fibres.

The medullated fibre descriptions are of material cut from the brain and cord after a few days hardening in 10 per cent. formalin and later put into Müller's fluid; afterward sections from these pieces were stained after the modification of Weigert's method described by Schaeffer.

Meninges. The characteristic lesion of the meninges—*i. e.*, the pia-arachnoid, is an infiltration of its meshes with cellular elements and proliferative and degenerative changes in its vessels, or a meningitis. The changes in the pia are so related with those of the vessels which lie in it that they will be considered together.

The meningitis shows local variations in its severity and in the character of its elements. In some places the pia appears quite normal; in others the meningitis is very intense. Generally the infiltration increases from a few cells lying in the deepest meshes of the pia to larger accumulations which distend the spaces and produce great thickening of the membrane. The greatest amount of infiltration occurs above and in the sulci. The exudate contains but little fibrin. The largest amount of fibrin, and this only a few threads, lies in an accumulation of polynuclear leukocytes in the region of a necrotic area. Where the exudate is least in quantity it is made up largely of lymphocytes arranged in a row compressed against the underlying cortex; among these are scattered a few plasma cells and occasionally an epithelioid cell, rarely a polynuclear leukocyte.

As the exudate increases in quantity the infiltrating elements spread into the upper meshes of the pia; epithelioid cells are here more common; plasma cells retain about the same relative proportion among the lymphocytes; polynuclear leukocytes are a little more frequently seen. In many places the exudate is so great that its cells lose all row-like arrangement and the meshes of the pia are torn apart; in these places the epithelioid cells not infrequently have inclusions of lymphocytes, usually one, but sometimes as many as six in a single cell.

There are places where focal accumulations of lymphocytes occur.

The exudate is always most abundant around the vessels and in these places shows the greatest variety among its elements. Plasma cells are always most numerous in the adventitia of the veins and here greatly outnumber the lymphocytes. Where the lymphocytes and plasma cells are intermingled, and in the exudate generally, it is possible to find, in sections stained by Unna's pyronin method, granules in the protoplasm of cells which in every other respect resemble lymphocytes; it is often quite difficult to distinguish between plasma cells and lymphocytes.

FIG. 1.

Vein in pia mater with necrotic nodule in the adventitia. Eosin-methylene-blue stain. Magnification 150.

The polynuclear leukocytes vary greatly in their distribution. Where the exudate is present in any considerable quantity they lie scattered at rare intervals. In some places they are in numbers and have a focal arrangement. This occurs in or near areas in which the tissues show necrosis, and is continuous with an infiltration of a vessel wall with leukocytes. There are a number of necrotic foci (Fig. 1); one appears as a knob-like mass projecting from the

adventitia of a vein. The media at this point is well stained but infiltrated with polynuclear leukocytes. The adventitia is in a characteristic necrotic state. The cytoplasm of its cellular elements stains poorly, and scattered everywhere through the area are nuclear fragments. Polynuclear leukocytes in various stages of disintegration are numerous. In these places there is a striking absence of lymphoid and epithelioid cells. With bacterial stains it was not possible to find any unquestionable micro-organisms. On the whole, apart from these focal areas where necrosis is present, the polynuclear leukocytes play little part in the meningeal exudate.

Arteries. The arteries of the pia show a variety of changes, the commonest of which is a proliferation of the connective-tissue cells of the intima; with this proliferation there is present an infiltration of the walls of the vessel.

In most instances the proliferation involves only part of the circumference of the intima. In a few arteries it extends completely around the lumen, but is then always of uneven thickness.

Not all of the vessels show changes, the majority appearing quite normal. The location of the arteries showing endarteritis seems to bear no relation to the intensity of the meningitis.

The endarteritis is not always present in those arteries around which the infiltration of the pia is most marked; and on the other hand, some arteries show severe endarteritis where the meningeal infiltration is very slight. The best general picture of the endarteritis is gained in preparations stained by Mallory's connective-tissue method. Normally the arteries of the pia, which are classed as of medium size, when stained by this method appear about as follows: bordering the lumen is a thin layer of blue fibrils, on which are red endothelial cells; this represents the intima, and follows the wavy outline of the underlying elastica, which appears as a homogeneous orange-red layer. Outside of the elastica is the media, with bluish fibrils interlacing among the red-colored muscle elements; external to this is the more or less broad layer of loosely arranged blue fibrils, or the adventitia.

The earliest changes in the endarteritis, in an artery of the same calibre, stained by the same method, are to be found in the inner blue layer, or the intima (Fig. 4). Where only a small segment of the circumference is involved in the proliferation, the remainder of the intima may not differ from the normal; but approaching the proliferated part, the endothelial cells of the intima together with a thin strip of the blue layer are loosened from the underlying homogeneous-appearing part which always remains in close contact with the elastica. The presence of epithelioid cells and an occasional lymphocyte beneath the loosened part seems to indicate that they have pushed the intima inward. Proliferation of the endothelial cells rapidly increases the thickness of the layer. Increasing number of epithelioid cells lie between the intima and the elastica

and push in among the proliferated fixed tissue cells. The cells of the intima at this point have the appearance of proliferating connective-tissue cells. They are spindle shaped, often branched, and the ends have a fringed appearance.

About these cells and interlacing among other elements of the proliferation are many blue-stained, connective-tissue fibrils. At the base of the intima there are other fibrils which are stained red or orange; for the most part these are coarser than the blue fibrils, but in a few places there are some that are more delicate and lie densely matted together. These latter red fibrils are probably fibrin.

The infiltrating elements beneath the intima and in the proliferation are for the greater part epithelioid cells; where the intimal proliferation is slight and the layer compact, a few lymphoid nuclei occur beneath the intima, but where the proliferated cells are loosely arranged there are many epithelioid cells. In a few instances quite large focal aggregations of epithelioid cells lie between the intima and the elastica.

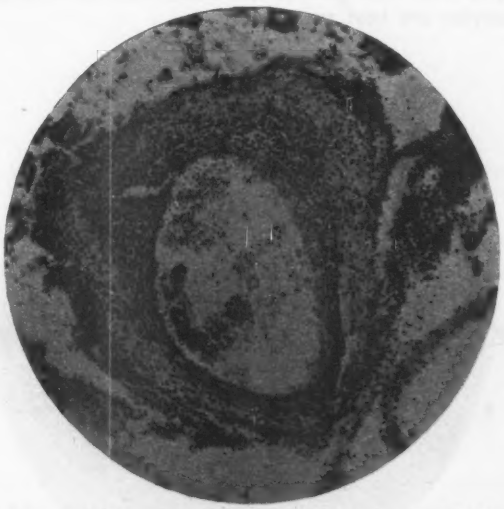
One artery, the intima of which shows extreme thickening, has a row of peculiar homogeneous masses, extending at least a quarter around the circumference. They lie deep in the proliferation near the elastica. The elastica, however, is plainly visible beneath in an apparently unchanged condition. These masses appear as confluent plaques of no characteristic shape. They stain brilliant red by Mallory's connective-tissue method, and deep blue with Weigert's fibrin method; these are apparently a degenerative product possibly of the newly formed connective tissue. Unfortunately there are no preparations which could determine whether or not they are of hyaline nature. Smaller amounts of this substance are present in a few arteries showing large proliferations of the intima. Close to this red area is a large, round, finely granular mass which remains unstained in all of the methods used.

The elastica in all preparations shows only slight changes. In some of the preparations by Mallory's connective-tissue method it is more of a yellow than a red color, and opposite these places the intimal proliferation is most marked. In a few instances there is splitting off of a few lamellæ from the inner border of the elastica, but there are no infiltrating elements beneath these and it is probably due to some irregularity in the sectioning of the vessel.

The media is not often involved. In a few arteries it is infiltrated with lymphoid cells; this occasionally amounts to small focal aggregations. Rarely one sees long-drawn-out cells as if they were migrating through the wall. The adventitia is more frequently affected than the media but less than the intima. The process is an infiltration and not a proliferation. In one artery which shows no trace of endarteritis there are lymphoid and plasma cells scattered through the adventitia. Those arteries showing the most marked

proliferation of the intimal cells generally show the greatest adventitial infiltrations. One artery shows swelling of the nuclei of the adventitial cells; these are pale and have an invaginated margin; among them are scattered nuclei, which are much larger than the pale forms; often these have threads of chromatin grouped in their interior; one nucleus shows a mitotic figure. There are very striking differences between these two varieties of cells. Sometimes there is a band of lymphoid and plasma cells on the border between the media and adventitia.

FIG. 2.



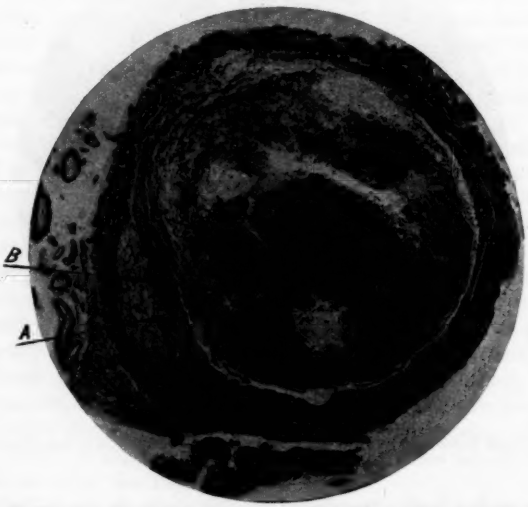
Vein in pia mater with swollen and infiltrated wall. Eosin-methylene-blue stain. Magnification 175.

A few of the larger arteries of the pia show at one point of their circumference a focal massing of polynuclear leukocytes, together with a few lymphoid and plasma cells. In most of these foci the form of the leukocytes is generally unchanged, but in some instances a focus is distinctly necrotic, the leukocytes staining poorly and their nuclei fragmented. In several arteries the necrotic focus is continuous with a similar focus in an adjacent vein. A number of these preparations were stained by methods for showing bacteria, and while in the débris there are scattered coccus-like particles, no significance can be ascribed to them, owing to the impossibility of here differentiating between organisms and nuclear fragments.

Veins. The veins of the meninges more generally show changes than the arteries. Commonly the larger veins are filled with red blood cells and relatively more polynuclear leukocytes than normal. In some there are threads of fibrin which in a few instances lie in

masses near the intima. The adventitia is usually infiltrated and its fixed tissue cells are swollen; these two processes give the vessel a somewhat increased size (Fig. 3). The infiltration, which is much greater than in the arteries, is made up of lymphoid and plasma cells, with a few epithelioid cells. In a few veins the walls are necrotic and at these places are densely infiltrated with polynuclear leukocytes; some of these latter contain inclusions of necrotic débris. The necrosis is more extensive than in the arteries and extends from the adventitia to the intima, but seems to be more advanced in the outer part of the wall, while next to the intima the leukocytes are best preserved.

FIG. 3.



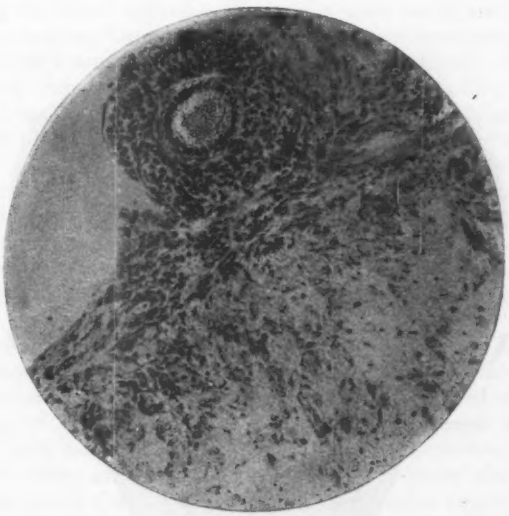
Middle cerebral artery. *A*, hemorrhage between media and adventitia. *B*, proliferated intima with adherent thrombus. Mallory connective-tissue stain. Magnification 30.

In the description of the meningeal exudate was noted the presence of a tumor-like mass, infiltrated with leukocytes, projecting from the adventitia of a vein (Fig. 1). The histological picture of this is not that of a gumma, but rather a focal massing of leukocytes at this point of the vessel wall, many of which have become necrotic.

In the gross examination of the brain, the left middle cerebral artery was thickened in its proximal part and was of a bluish-black color (Fig. 4). Sections across the artery at this point show great proliferation of the intima with a thrombus partially occluding its lumen. The proliferative changes in the intima are quite like those above described, excepting for some differences in the infiltrating elements; scattered among the proliferated intimal cells are many

polynuclear leukocytes and epithelioid cells. These latter usually have inclusions of yellow pigment; in some of these are red blood cells which still preserve their normal outline yet will not stain with eosin. The greater number of these phagocytes lie deep in the intima, near the elastica. Adherent to the proliferated intima is a thrombus composed for the larger part of a fine, granular-appearing substance which stains poorly; in this are many branched fibroblasts and a few epithelioid phagocytes. In cross section the thrombus fills a little more than one-fourth of the lumen; the remainder of the space is packed with red blood cells, among which

FIG. 4.



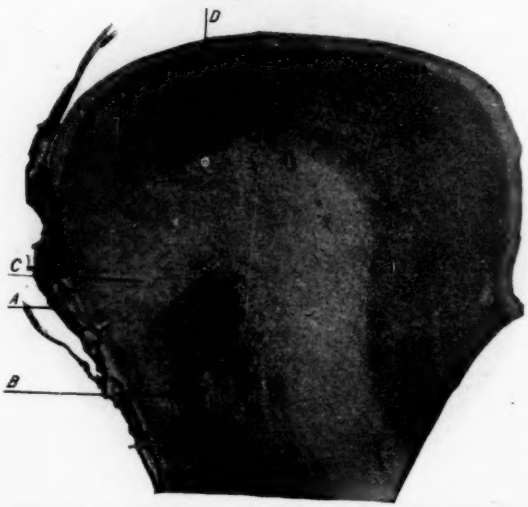
Hypertrophy and hyperplasia of glia cells in the superficial layer of the cortex. Adherent to the cortex is a piece of pia mater with a swollen and infiltrated vein. Nissl stain. Magnification 100

are fibroblasts and scattered small clumps of fibrin. There are a few epithelioid phagocytes with inclusions of yellow pigment or pale shadows of red blood cells. The media of this artery, excepting for a small segment, is of loose structure, and contains a number of infiltrating cells; some of these are long, compressed forms as if in process of emigration. The infiltration is very abundant at the point of attachment of the thrombus. At the point where the intimal proliferation is greatest there is a small hemorrhage between the media and adventitia, and both adventitia and media here show their greatest infiltrations; polynuclear leukocytes are quite numerous and often show necrosis.

It seems best to describe the changes in the brain substance according as they are diffuse or focal.

As diffuse changes in contradistinction to focal are included, those changes in the brain substance occuring apparently independent of foci of encephalitis or hemorrhages. It is not possible to place sharp distinctions between the two processes, as diffuse processes show greater intensity at some points than at others. The diffuse process is characterized by degenerative changes in the nerve cells, and by degenerative and proliferative changes in the glia and vessels. No section of the many examined is free from changes, although in the majority they are very slight.

FIG. 5.



Frontal convolution. *A*, pia mater. *B*, area of encephalitis. *C*, bordering zone in which nerve cells have been destroyed and where glia and non-nervous elements show proliferative changes. *D*, comparatively uninjured nerve-cell layers. Nissl stain. Magnification 10.

Low Magnification. In most sections there is present a hypertrophy and hyperplasia of the glia cells of the superficial layer of the cortex. The degree of this varies greatly, at some points being more marked than at others. The progressive changes in not a few places are so great that the contrast between superficial layer and nerve cell layers is obliterated (Fig. 3).

Sections from regions but slightly changed show no disturbance of the normal cortical architecture. In regions severely altered there are patches from which the nerve cells have disappeared, and those which remain appear shrunken and severely diseased (Fig. 5).

In these latter regions the substance between the nerve cells is strewn with disintegration products of nerve cells and obscured by the swelling of the glia cells.

High Magnification. Sections from the regions least altered show only slight disintegration of the Nissl bodies of the nerve cells. Many nerve cells are quite normal.

In the more severely altered regions, such as those showing under weak magnification evidences of nerve cell destruction and disappearance, there are present a variety of changes in the nerve cells. Two of these changes are so characteristic and occur so frequently that one seems justified in regarding them as of especial importance in the general process present in the brain.

Among the nerve cells of such a region there are numerous dark, shrunken, angular forms, the apical process and dendrites of which are traceable a considerable distance from the cell body; the axone is similarly stained. Internally these cells present a fine, crumbly structure; no distinct Nissl bodies are to be made out; many cells appear to be filled with a fine, pale dust; others may be described as finely vacuolated or honeycombed. In a few cells no trace of cell structure lies between the nucleus and the cell wall. The nucleus is generally pointed; although in some of the cells the nuclear membrane is fairly well outlined, in the majority the membrane cannot be differentiated from the deeply stained homogeneous nuclear ground substance. The nucleolus has a tendency to assume irregular shapes.

Scattered among the nerve cells of such a region are dark-blue, homogeneous nuclei, about which lie pale granules; these are evidently end stages of cells destroyed in the above type of alteration. This type of change rarely is distributed all through a region, occurring only where the cortical changes are most severe. Among or not far from such cells commonly occur others showing an entirely different type of alteration. Forms quite similar to this type occur among the nerve cells persisting in or bordering foci of encephalitis.

In the second type of alteration the nerve cells are swollen; the dendrites and axone are traceable far from the cell; within the cell the granules have disappeared, leaving the cell body filled with a pale meshwork; this latter is sometimes so faintly visible that the cell has almost a homogeneous appearance. The nucleus usually presents a pale-blue, homogeneous appearance and its membrane is invisible. In a few instances the nucleus is indistinctly mottled. Frequently two or more coarse granules, staining an intense blue color lie within the nucleus. In some cells the nucleus becomes irregular in outline, and as the granules within the cell disintegrate it fades away. The nucleolus takes on a mulberry-like form. Ultimately all traces of the cell structure disappear. Not infrequently these cells show deeply stained particles of substance lying

on or about the cell; sometimes these are massed at the base of the cell or at the tip of the axone. These are what Nissl regards as degenerations, and as incrustation upon the pericellular net.

This last type of alteration is not a common one. In no other cortex have we seen it in such numbers. It is a very severe condition and is always associated with various end changes of the same general type of alteration.

In addition to these two types of cell changes there are isolated examples of Nissl's "grave alteration," a type of alteration in which the body of the nerve cell breaks up into small characteristic ring-like degeneration products, the nucleus atrophies, and finally the entire cell disappears. There are a few cells which show the experimental axonal reaction; this is characterized by swelling of the cell with disintegration of the Nissl bodies, always more marked at one side of the cell. The nucleus, at the same time, takes a position close to the wall.

While the alterations among the nerve cells are varied and apparently all of a regressive character, the glia cells, excepting in a few places where the tissue injury is extreme, show progressive changes of a constant character.

There is a good deal of uncertainty as to just which of the nuclei present in the cortex are glia elements; there are, however, certain forms which are easily identified and which, in their progressive development, show constant characteristics in their transitions up to forms which are unquestionably glia cells.

The earliest stage in these progressive changes is swelling of the nucleus with an increase in size of its contained chromatin granules. At the same time there is noticed, spreading around the nucleus, a substance characteristic in its peculiar speckled or granular appearance. In the further development this substance becomes more compactly arranged about the nucleus and assumes the form of an oblong or oval cell body with radiating, process-like extensions; the nucleus takes an eccentric position, bulging from one side of the cell; gradually the granular appearance changes to one more homogeneous; from this stage the tendency is to shrink into what one regards as of the ordinary astrocyte type. This cell in some of its stages is probably the fibre-producing form. In satisfactory preparations there are increased numbers of glia fibres where these types occur, and it is often possible to demonstrate fibres still attached along the sides of the cell body or processes.

Progressive changes occur among some of the glia cells in the superficial layer of the cortex in every section examined. The intensity of these changes varies greatly; while generally the glia cells are rather evenly distributed through the superficial layer in any one section, there may be in the same section a focal increase of cells which sometimes fills the entire thickness of the layer (Fig. 3).

The glia cells of the superficial layer show more fully developed forms than those of the nerve cell layers, excepting where there are areas of severe tissue injury. The changes present in this layer appear to be intimately related to the changes in the pia mater. Where the meningitis is most intense there occurs the greatest reaction in the underlying glia cells, and where the meningitis is slight the glia reaction is not marked and is confined to the upper margin of the layer. Similarly, where there are areas of encephalitis lying in the more superficial part of the cortex there is always seen a marked glia hyperplasia.

In these areas of focal accumulations of glia cells, and where the glia cells have large cell bodies, it is always possible to demonstrate with elective staining methods that the glia fibres are also increased.

The glia cells of the nerve-cell layers show earlier and less intense changes than those of the superficial layer. No section is free from changes. In regions which show no foci of encephalitis the cell body is rarely completely developed, the cells showing the earlier progressive changes. Where the alterations in the nerve cells are slight, there occur swollen glia nuclei lying in a mass of delicately speckled protoplasm; sometimes these lie in groups of two or three. Where the nerve-cell changes are severe, and where the ground substance of the cortex is strewn with the débris of disintegrated nerve cells, the glia cells show the more advanced changes. There are a few places where the whole cortical structure shows severe injury, and in these there occur among glia cells showing progressive changes dark nuclei, which are apparently regressive forms of glia cells.

The distribution of the glia changes in the nerve-cell layers is peculiar. There is an unevenness in their distribution and a tendency toward focal variations in intensity. In a few areas where the nerve-cell changes are very severe, many cells having disappeared, the glia changes are very slight.

There occur in the cortex other forms of nuclei, the nature of which are not at all certain. One of these is a long, spindle-shaped cell, which Nissl calls a "Stäbchenzelle;" this is present in almost every region studied and appears as a long nucleus with coarse chromatin granules and filaments of cell-body substance projecting from either end. These cells will be described later.

Another form is the satellite nucleus; these are so few that they apparently play no part in the process present. There is one point which may be of interest, and one which is often illustrated in other processes, namely, that these satellite nuclei show no changes in regions where the glia nuclei show the most characteristic progressive alterations.

Other types of nuclei present in the nerve-cell layers are related to focal processes and will be described in that connection.

In general, it can be said that these changes in the glia cells are more delicate indications of the changes present in the cortex than

are the changes in the nerve cells. In some regions where it is not possible to regard the nerve cells as altered, the glia cells show distinct though very early changes.

The white substance of the cortex shows these diffuse changes to a far less extent than the nerve-cell layers. Those changes which one finds in the glia nuclei are apparently always of a focal character, dependent either upon vascular lesions in their neighborhood or they are reactions secondary to foci of encephalitis in the overlying nerve-cell layers.

Bloodvessels. In the regions showing more or less diffuse alterations, two apparently different changes are seen in the bloodvessels. These two types are: 1. Infiltration of the vessel walls and perivascular spaces. 2. Swelling of the vessel walls.

1. *Infiltrations.* The vessels which extend in from the pia frequently have an extension of the pial infiltration into their walls and perivascular spaces. The distribution of these infiltrated vessels is peculiar; they occur in regions showing only slight changes in the cortex and in the neighborhood of vessels showing no infiltrations whatever. Rarely do they extend deeper than the upper nerve-cell layers. They are most common in the superficial layer at the bottom of a sulcus.

The infiltration in and about a vessel wall is never very great. Generally there are only a few nuclei present. In this infiltration there occur lymphoid and plasma cells, epithelioid cells, with inclusions of pigment, and rarely a mast cell. These cells lie in the adventitia and perivascular space. Sometimes lymphoid cells alone are present, and sometimes only plasma cells, more generally the two occurring together.

Occasionally there are infiltrations of the walls of vessels lying deep in the nerve-cell layers and which show no connection with the pia, at least, not in the plane of the section studied; there is no uniformity in the distribution of these vessels.

In no way can it be seen that these infiltrations differ from those associated with general paralysis, either in the character of their constituents or in their localization in the vessel walls. In most cases of general paralysis, however, the infiltrations are larger, but there often are cases in which they are not more marked than here.

2. *Swelling of the Vessel Walls.* This is a change present in varying intensity in every region studied; it is always less marked where the changes in the nerve cells and glia are slight and is greatest where these are most severely altered. As this process is nowhere as marked as in the lesions of focal encephalitis, it will be better to describe it later on in that connection.

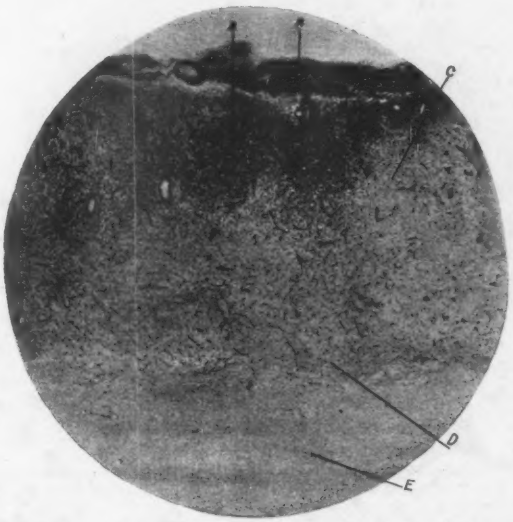
Focal Changes. As focal changes, there occur in the brain: 1. Areas filled with the elements characterizing granulation tissue or areas of encephalitis. 2. Changes of simple necrosis or softening, directly related to a vessel in their immediate vicinity. 3. Hemor-

rhages. 4. A few foci, which, from their compactness and similarity to the histological picture of a gummatous tumor, are so regarded.

In all of the focal processes it is necessary to discriminate between the primary process and various reactive changes in the elements bordering the focus. It is difficult to judge as to the relative or absolute number of these various focal processes. In the fresh brain it was not possible to identify the smaller foci, but after hardening in formalin many were picked out from their more or less marked contrast with the surrounding tissue.

As encephalitis we here describe a process characterized by death of the nervous elements proper, proliferative changes in the vessels,

FIG. 6.



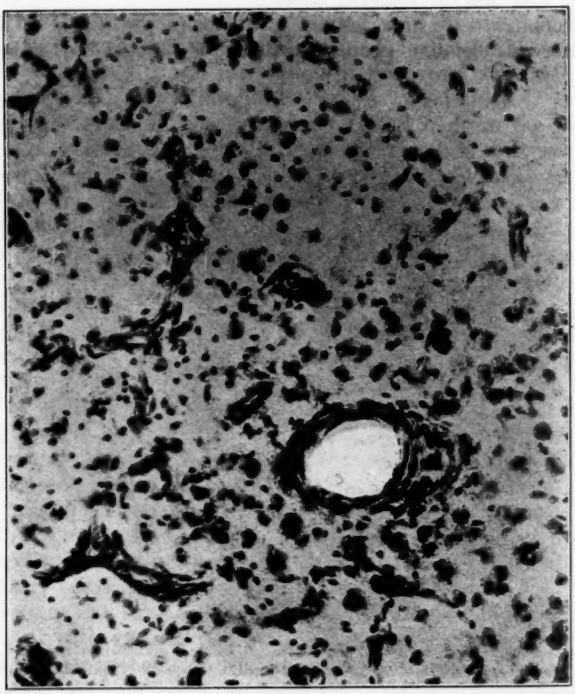
Area of encephalitis. *A*, infiltrated pia mater. *B*, focus of granulation tissue. *C*, zones in which glia and non-nervous elements are proliferating. *D*, layer of epithelioid cells lying along the edge of (*E*) white substance. Nissl stain. Magnification 15.

and an infiltration of the area with epithelioid cells. Accompanying this process there are always reactive changes in the glia. The area is separated from regions in which the elements, while not normal, preserve much of their integrity by zones in which the elements show reactions differing according to their distance from the focal process.

It is not demonstrated that any of the foci are direct invasions of the process from the pia mater. In some instances, while the infiltration of the pia mater and that of the underlying cortical substance appear to merge into each other, on careful examination a difference between the two processes is seen. This is principally in the char-

acter of their elements. In the pia the predominating cell is the lymphocyte, while in the underlying cortex it is the epithelioid cell which occurs in greatest numbers, lymphocytes being quite rare. The upper part of the superficial layer of the cortex contains strikingly fewer cells than the regions on either side and forms a boundary zone between the dense infiltrations of epithelioid cells below and the meningeal exudate above.

FIG. 7.



Epithelioid cells and swollen vessels from the outer edge of encephalitis area. Nissl stain. Magnification 225.

Each of the larger foci of encephalitis is limited primarily to the nerve-cell layers of the cortex. In some instances it involves all of the layers; in others its upper level reaches the position of the layer of small pyramidal cells. (Figs. 6, 7, 8.)

In the earlier stages of the process these areas of encephalitis are separated from the white substance by a border of closely packed epithelioid cells. Later this sharp demarcation is less prominent. The focus is bordered on either side by zones in which there is a

reaction differing in intensity according as they lie close to or removed from the focus. One of these foci, under low magnification, shows the normal cortical architecture entirely changed. Nerve cells are not to be distinguished, and the area is filled with swollen vessels and pale cellular elements (Fig. 7). Under the immersion objective not a normal nerve cell can be seen. Here and there lie dark cells, which, from their general appearance, seem to be the remnants of former nerve cells; such also are scattered, shadow-like pyramidal forms, which have a faint yellow tinge.

FIG. 8.

Frontal convolution, the entire area showing encephalitis with almost total destruction of nerve elements. Nissl stain. Magnification 15.

Most striking in one of these foci are the swollen bloodvessels and the large numbers of epithelioid cells crowding the area. All of the bloodvessels are swollen; as their individual cells increase in size and become broader, their protoplasm has a tendency to stain deeper. In some cells the protoplasm has a granular appearance and is usually more dense at one pole of the cell; this part of the cell stains an intense blue color in Nissl preparations. The nucleus increases in size; its interior has a glassy, homogeneous appearance and rarely is it possible to distinguish the chromatin network. The nucleolus is large and of a characteristic blue color; often its outline is oblong or otherwise irregular; occasionally there are from one to three small, deeply stained granules scattered around the nucleolus.

This swelling of the cells of the walls gives the vessel a laminated

appearance. It occasionally seems as if the vessel is a mere nest of concentrically arranged cells. The lumen is almost obliterated; sometimes a leukocyte or red-blood cell is pushed in among the cells of the walls. The normal compact structure has become loosened and the cells are pushed apart. Some vessels cut in their long direction seem as if their walls are split into two layers. A few of the cells show mitosis. The relation of these swollen cells of the vessel wall to the epithelioid cells abounding in their neighborhood is interesting. In the process of swelling some of the outer cells of the wall become loosened at one end; this end is often noticed projecting free from the wall. While the cells which belong positively to the vessel wall are compact and lack the spongy or vacuolated appearance of the free epithelioid cells, it is common observation that as soon as a cell shows indications of loosening from the wall of the vessel its protoplasm appears less compact. It seems quite possible to trace all stages between the swollen cells of the outer parts of the vessel wall and the epithelioid cells lying free in their neighborhood.

It is notable that the epithelioid cells are most numerous near those vessels which are most swollen; while around the vessels in the peripheral parts of an area of encephalitis they are not found in large numbers. Some of these swollen vessels, notably the larger, have lymphoid and plasma cells crowded in among the cells of their walls, and in places appear quite the same as the infiltrated vessels in other parts of the cortex where the tissue injury is less marked. From the study of this and similar foci, it seems as if the swelling of the walls and infiltration are two separate processes, the latter process being more chronic.

The epithelioid cells crowding the focus of encephalitis for the most part do not differ from those found in the areas of inflammation of other organs. They are the "Körnchenzellen" of German descriptions and correspond to the cells which abound in the early stages of anæmic softening of the brain. There are some cells present in considerable numbers which show a great variety of form; the body of these cells is sometimes long, with branching protrusions from one end, or a part of an irregular-shaped body may be extended like the pseudopod of an amœba. These cells are always coarsely vacuolated; in some there are yellow-tinged inclusions; many have large spaces, like digestion vacuoles. What these cells are is difficult to decide.

Another type of cell occurs in few numbers in the central part of the areas of encephalitis, but is very numerous in the bordering regions. About one of these foci it is distributed in ill-defined zones, in each of which it shows phases of development different according as they are near or far from the parts showing the more severe general tissue changes. In regions more or less removed from areas of encephalitis, where only slight general changes are noticed in the nerve cells and glia, there occur scattered in few numbers long pale

nuclei, with a rather indistinct, filament-like cell body extending from either end. These nuclei are oblong or fusiform; in Nissl preparations they stain more of a greenish color than the ordinary glia nuclei and contain a number of coarse chromatin granules. The cell-body substance is slight in amount and finely granular in structure. In this stage it corresponds evidently with what Nissl describes as the "Stäbchenzelle," a form occurring frequently in the cortex of general paralysis. Nearing the focus of encephalitis there is an increase in the number and size of these forms; they have become longer and broader; the cell body is coarsely meshed and vacuolated; along the edge of a focus of encephalitis there are branched forms, apparently of the same element; the cell wall is here sharper outlined; the nucleus appears to be placed nearer to one side, and the cell body becomes more loosely partitioned and seems to be in a process of channelling through. Often two or more will be joined at their ends or at the tip of a branch. In a few instances it seems as if they are directly connected with the wall of a delicate vessel. It is difficult to decide what the origin and function of this type of cell are. The cells differ in so many ways from glia elements that it seems certain that they are not of this class. They are also not of the type of the common epithelioid cell. There are evidences that they are related to the process of forming new vessels, but no positive conclusions can yet be stated. We have seen this form and the large branched vacuolated phagocyte cell in simple encephalitis after trauma, and the former is not uncommon in various organic brain diseases, notably general paralysis, where the formation of new vessels is often quite prominent.

Other cellular elements present in one of the foci of encephalitis are glia cells in various progressive stages. Most of these show hypertrophy of the cell and nucleus. The nucleus is large, containing coarse chromatin granules and lying at a corner or side of a more or less homogeneous cell body, from which project short, stubby processes. In these foci the glia cells are always fewer than in the bordering regions; in the older parts of the focus the glia cells are shrunken and present the form of the common astrocytes.

Scattered through the focus are various nuclei difficult to identify; some are like the lymphoid nuclei occurring elsewhere. Many are nuclei apparently regressively altered. In preparations by Nissl's method these appear as dark-green nuclei of irregular outline, and usually of a homogeneous structure; in some it is possible to distinguish a few dark granules. Polynuclear leukocytes are very rarely seen.

The areas of encephalitis are bordered by zones which show changes different from those present in the area itself, and are a combination of the changes which we have described as diffuse and those caused by reaction secondary to the encephalitis (Fig. 6, c).

Each focus is bordered by a zone in which nerve cells are few;

great numbers of them have disappeared, and those remaining are in various regressive changes leading to complete destruction of the cell.

The vessels are swollen and show proliferative changes, which are, however, never as prominent as in the focus itself. Many show the adventitial infiltrations seen all through the cortex. In this zone lie large numbers of the peculiar long cells described earlier. Epithelioid cells are few and lie close to the margin of the focus and always alongside of a vessel. Hypertrophied glia cells are numerous; these have swollen nuclei, always of a characteristic glassy appearance, and differing in this stage from all the other nuclei present; the nucleus contains one or more coarse lumps of chromatin; surrounding the nucleus is a protoplasmic body; in the greater number of cells in this zone this appears as a large, bulging, homogeneous mass with short, stubby processes. In the older of these the border seems to take a deeper stain than the rest of the body. This type represents the fully developed hypertrophied cell, and between this and the earlier progressive changes there are all stages. Some of these cells have two nuclei; none show mitosis. There are a few glia cells occurring in places where the tissue injury is most severe, which have swollen, loosely-meshed cell bodies, which stain poorly; occasionally there are the peculiar forms of glia which Nissl calls "Gliarasen." These are "mould-like" masses of spreading protoplasm, in which lie clusters of glia nuclei.

The white substance of those regions where the cortex shows focal encephalitis has hypertrophied glia cells close to the focus. Only one region, and this where several foci are in one section, shows diffuse changes throughout the white substance. In this region hypertrophied glia cells are scattered everywhere. There are also many of those shrunken, dark, homogeneous nuclei described earlier as occurring in the focus itself. Epithelioid cells occur in moderate numbers. Close to the focus there are swollen vessels and delicate, newly formed capillaries.

In general, the vessels of the white substance are less altered than those of the nerve-cell layers. Occasionally there are infiltrations of lymphoid and plasma cells in their walls.

2. Areas of anæmic necrosis due to vessel changes—*i. e.*, simple softenings. Apart from the areas of encephalitis, there are several regions which show the characteristic process of softening; these lie always in the course of the vessel, visible in the plane of the section. They are only seen along the deep or medullary arteries. One such focus of softening borders an artery extending through the nerve-cell layers into the white substance; around the vessel the tissue is of loose structure and infiltrated with epithelioid phagocytes. Formalin-fixed preparations stained with Scharlach R. show that these cells are crowded full of fat or myelin granules. The glia bordering these areas of softening always shows progressive changes. In a

number of places away from the foci of tissue injury the epithelioid cells in the adventitia or perivascular infiltration contain granules giving the reaction of fat.

3. *Hemorrhages.* There are no focal hemorrhages in the cortex. In the left internal capsule and in the left thalamus there are small punctate hemorrhages. Among the pyramid fibres in the right side of the pons there are a number of larger hemorrhages. Several smaller hemorrhages are present in the medulla. The nuclei of the ninth and tenth nerves on both sides are infiltrated with blood. In all of these regions the bloodvessels are intensely engorged; some of these are ruptured and their neighborhood is infiltrated with blood cells. Around one of these hemorrhages in the medulla the tissue is porous, such as occurs in early softening, but there is no demonstrable reaction of the fixed tissue cells. Always near these areas there are many round-shaped or irregular-shaped myelin bodies; there are no epithelioid phagocytes. The red cells have their forms well preserved and stain deeply with eosin. These facts seem to show that the hemorrhages present are very recent.

4. *Foci Resembling Gummatous Tumors.* Excepting for the focus of necrosis noticed in the walls of some of the meningeal vessels, there is nothing resembling a gumma in the brain above the medulla.

In the medulla there are several foci which in their histological picture correspond to gummata and differ essentially from the other focal processes described. One of these is in the pia around the root of one cochlear nerve. Here there is a focal accumulation of densely packed epithelioid-like cells, with many polynuclear leukocytes in the central part. The area stained poorly; many of the cells show characteristic necrosis. The mass of cells spreads into the pia along the course of the nerve and many push in among the nerve fibres.

A section passing through the lower part of the olive shows five small focal cellular accumulations in the gray substance around the central canal. These are composed of closely packed cells, having pale nuclei with coarse chromatin granules. These nuclei are of a variety of shapes; some are oval, or flask-shaped, or sharply bent at their middle. Most of the nuclei are bordered by a broad rim of protoplasm. These cells differ from those of the infiltrations of the vessel walls of this region; these latter always resemble lymphoid and plasma cells, while those of these foci are of the type of epithelioid cells. It seems probable that these are specific gummatous tumors.

Medulla and Spinal Cord. The pia shows an infiltration differing only in intensity from that of the convexity of the brain. Vessel changes are, however, more general. The majority of vessels are engorged with blood. Many have perivascular infiltrations; many show proliferative changes in the intima and adventitia. One artery in the region of the medulla has endarteritis and occlusion of its lumen by a partially organized thrombus. A few vessels show areas of necrosis in the media and adventitia similar to those found in the

meninges of the brain. It is not demonstrable that the meningitis is more marked at any special level of the cord further than that where the nerve roots are most abundant and the pia of loosest texture, as in the lumbar and sacral levels, the meningitis is more prominent than in other regions.

The walls of the vessels in the medulla are more generally infiltrated than those of the brain. Not only the vessels extending in from the pia, but those lying deep in the more central parts show larger accumulations of lymphoid and questionable plasma cells in their walls and perivascular spaces. The focal hemorrhages occurring here have been noted. Along almost the entire length of the medulla and cord the glia cells of the margin are hypertrophied. At one point there is a triangular area of hypertrophied glia cells extending deep into the medulla. There are no signs of an inflammatory process in this area.

Satisfactory preparations of the cord by Nissl's method show remarkably well-preserved nerve cells. Besides the hypertrophy of the glia cells around the margin there is a slight degree of infiltration of cells from the pia around the arteries and posterior root fibres.

In a section through the cervical cord there are present two small foci in the gray commissure in which the glia cells are hypertrophied.

Many sections from the medulla and cord prepared by methods for demonstrating the myelin sheaths show no fibre degenerations. Marchi preparations show scattered, blackened fibres among others which appear normal. These latter findings are so uncertain that they are not regarded as important.

Fibre Degenerations of the Cortex. Preparations were studied from many different regions, but only one of those shows any coarse fibre degenerations. This was from the left gyrus rectus (Fig. 9).

Even without magnification, there is noticeable a striking paleness of part of the white substance. When more highly magnified, the degenerated part appears to involve about a third of the white substance.

It is clearly demarcated from the normally stained part, but from this latter there passes into the degenerated part some fibres, either singly or in sprays, which are well preserved. The degenerated portion is made up of pale, barely visible fibres, among which are scattered a few that are well stained. It is easy to find evidences of degeneration among the fibres along the edge of the more normal part, principally flask-like bulgings of the fibres; these are also present in those stained which lie scattered through the degenerated area. In this section there are present in the nerve-cell layers two small and one larger area in which the nerve fibres are absent; each of these is bordered by fibres relatively as numerous as in other regions at this depth. Each of the areas show severe general tissue changes, and contain dark nuclei and an increased number of capillaries, which are much

engorged. In every way these agree with foci of encephalitis, as seen in more suitably prepared sections.

Above on either side of these areas there is a very distinct thining of the tangential fibres. The larger of these foci lies directly above the part of the white substance from which the fibres have disappeared. Between the focus and the white substance only a few pale, radiating fibres remain.

While this is the only region which shows coarse changes, several others show finer degenerations.

FIG. 9.

Gyrus rectus. The fibres in the left half of the white substance degenerated. *A*, focus of encephalitis. *B*, area of fibre degeneration. Myelin sheath stain. Magnification 10.

In the right frontal convolution the tangential fibres of the superficial layer are in places reduced to a few isolated fibres, and at some points are entirely interrupted. In these defective places there is always noticed hypertrophy of the glia cells. The pia at this point also shows an intense infiltration. In this section, as in all of the others, it seems true that in this layer where the glia cells are hypertrophied the superficial tangential fibres are fewest.

In the left first frontal convolution there is a similar disappearance of the tangential fibres in the superficial layer. The same is true of the left and right anterior central convolutions. In the occipital regions no change is noticed in the fibres.

In analyzing the case the early occurrence of the disease of the nervous system is of clinical interest. In many of the text-books it is stated that syphilis of the nervous system is a phenomenon occurring late in the disease. There have, however, been a number of analyses of large series of cases, notably by Naunyn,[1] Gowers,[2] and Hjelman,[3] as well as a number of isolated cases, which show that syphilis of the nervous system often occurs within a few years or even within the first six months after infection (Oppenheim[4]). In our case the first nervous symptoms occurred within six months, and the entire course was completed in eight months after infection.

Anatomically, syphilitic disease of the central nervous system may manifest itself as: 1. Gummata. 2. Chronic hyperplastic inflammation. 3. Disease of the bloodvessels. To these may be added the parasyphilitic processes, such as those of tabes and general paralysis. It is not uncommon for all of these three to be present at the same time, and multiformity is quite characteristic of syphilis of the nervous system. This is notable in the present case.

In this case the most striking anatomical changes are those of the bloodvessels, while the production of focal gummata forms only a minor part of the process. In most of the reported cases of early syphilis of the nervous system lesions of the bloodvessels are more marked than focal gummata. Kahane[5] states that the diseases of the brain which occur in the early period of syphilis have the common anatomical character of almost always involving the bloodvessels, while gummata in the central nervous system, as well as in other organs, tend to occur late in the disease.

The meningitis present is a diffuse process and shows only a few questionable characteristics which would entitle it to be classed as a gummatous meningitis, the form which syphilis of the pia mater usually takes.

In its distribution and in the character of its elements it shows nothing specific. The great predominance of lymphoid and plasma cells and the rarity of polynuclear leukocytes give it the character of a chronic inflammation. These same elements are those which make up the meningeal exudate in general paralysis. It seems probable that the lymphoid and plasma cells appear first in the meningeal exudate, and that the occurrence of epithelioid cells and the few polynuclear leukocytes are related to differences in the severity of the tissue injury or of focal lesions of the coats of the bloodvessels. These latter cells are always found near vessels or where the exudate is in such quantity and the fixed tissue elements injured to such a degree that it is impossible to judge as to the source and the relation of the various cells to the primary process.

So far as can be determined, the cellular elements of the exudate differ little from those occurring in tuberculosis of the meninges; they, however, differ essentially from those of the acute infectious meningitides.

The intergrading forms of lymphocytes and plasma cells are interesting as showing the apparent close relationship of these elements.

Lesions of the bloodvessels are the commonest constant finding in syphilis of the central nervous system. According to Nonne,[6] they are seldom absent. Of the lesions, the endarteritis is the most familiar. In this case it is possible to study the process in an early stage. The first demonstrable step in the endarteritis is the lifting of the intimal endothelium by cells which pass in between the intima and elastica; the intima proliferation is secondary. Where these infiltrating elements came from was not determined. It is probable that they have wandered in from the adventitia, which in almost every instance shows local inflammatory changes. It is striking, however, how little the media is involved, as only rarely is it infiltrated, or can cells be seen which are in process of migration. The necrotic changes are always in the outer wall and spread from there inward. This necrosis is not unlikely the result of changes in the nutrient vessels of the adventitia. These findings accord with the position of Köster,[7] Friedländer,[8] and perhaps the majority of investigators, who regard the process as one spreading from the nutrient vessels toward the intima and do not regard the process as specific for syphilis; on the other side, Heubner[9] described the proliferation of the intima as the primary change due to direct action of the infectious agent of syphilis, the changes in the outer walls being secondary.

The thrombosis of the middle cerebral artery is apparently very recent. The intimal proliferation is not seen in the veins, but commonly there is present a mesophlebitis or periphlebitis. In the veins it is certainly noticed that the inflammatory process spreads from without toward the inner coat.

The pathological process in the brain and cord is characterized by multiformity. In the brain there is present a diffuse degenerative process affecting the nerve elements, glia and bloodvessels throughout the whole cortex. Apart from this, there are disseminated areas of encephalitis; these latter are apparently not dependent upon changes in the meninges. They show the phenomena of early granulation tissue, as well as local degenerative changes in the nervous elements and secondary reactive changes in the glia.

The hemorrhages, focal softenings, and the questionable gummata present are processes independent of these areas.

In its entirety the process may be classed among the few described cases of disseminated syphilitic encephalitis, as the inflammatory nature of the process seems to be the most prominent feature.

The frequent involvement of the meninges with lesions of the brain tissue has given the name meningo-encephalitis to a variety of

syphilitic processes of the central nervous tissue. In the strictest use of the term, it has been applied to those processes where the inflammation spreads into the brain tissue along the bloodvessels from the meninges. In some instances it has been given to cases where there was present a meningitis with a gliosis of the underlying adjacent brain tissue; in others where a meningitis was associated coincidently with a process of simple softening. Apart from these, there are a few cases in which, in addition to a meningitis, there is present an independent inflammatory process in the brain tissue.

There is a good deal of confusion in the conception of encephalitis, and it is difficult to interpret many descriptions in the literature. This is true not only of syphilis, but of other brain diseases. The term encephalitis has been commonly applied to lesions which are those of an anæmic necrosis or simple softening. In other instances the description is that of a gliosis rather than an inflammatory process.

One is justified in regarding the process as one of syphilitic encephalitis where there occurs in syphilitic brain disease inflammatory phenomena in the brain substance independent of gummata, and not secondary to hemorrhages or the necrosis due to vascular obstruction.

Heubner,[10] in 1876, found, among some 150 cases of syphilis of the nervous system, 36 cases in which the process was regarded as one of simple inflammation. A careful analysis of 22 of the best of these descriptions convinced him that there was not a single case up to that time which could be regarded as a simple inflammation independent of a new-growth. In none of these cases was the histological examination thorough. In a few cases the inflammation might be ascribed to softenings in the neighborhood of a focal gumma overlooked during the examination. In many the inflammation was associated with meningitis. The remaining must be described as due to vessel disease, not focal.

It has not been possible to review all of the cases described as syphilitic encephalitis since Heubner's work. Many of the descriptions of the histological findings are incomplete, or no distinction has been made between the process of softening and that of an independent encephalitis. In others the phenomena of focal encephalitis are either described as extensions from the meninges or differ in essential ways from the case we have described.

A classical case often quoted in the literature is that of Charcot and Gombault,[11] in which there was present, in addition to focal gummata, independent areas of chronic inflammation. In the monographs of Bechterew[12] there are descriptions of a few cases which are regarded as encephalitis, independent of meningitis.

The best of these descriptions are cases of Oppenheim, Jürgens,[13] and Bechterew. In Oppenheim's case there was a focus of inflammation about 1 cm. in diameter in the pons and posterior corpora

quadrigemina; the brain arteries were normal, and he designates the case as one of encephalitis.

Jürgens has described a case in which at death there were signs of secondary encephalitis. At the autopsy there was found an acute universal encephalitis. He regarded the disease as exceedingly rare.

The most complete description we have found is a case of Bechterew's.[12] This case in its histology resembles our own case very closely. The course was somewhat longer. The first symptoms developed in the year following infection, and death occurred two years later. He names the case one of disseminated syphilitic focal sclerosis, and adds that it is the only case of this type which has been completely studied, both clinically and pathologically.

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SOME OBSERVATIONS ON THE EFFECT OF ALTERNATING CURRENTS OF MODERATE FREQUENCY ON DOGS.

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THE extensive and accurate researches of Prevost and Battelli[1] leave little to be investigated as to the effects which follow, and the cause of death from the application of commercial electrical currents to animals. We think it desirable, however, that we place on record

[1] Journal de physiologie et de pathologie générale (1) 1899, tome i. p. 399; (2) p. 427; (3) p. 689 (4) 1900, tome ii. p. 755; (5) 1901, tome iii. p. 1085; (6) p. 1144.

some observations which we have had the opportunity of making on the effect of alternating currents of high frequency on anæsthetized dogs; the more so, since we believe that the observations throw some light on the cause of the variable lethal effect of such currents.[1]

Previous to Prevost and Battelli's papers considerable confusion existed as to the exact cause of death from electrical currents. d'Arsonval[2] and Kratter[3] ascribed death to respiratory cessation from paralysis of the bulbal centre; whereas, Tatum[4] and Biraud,[5] thought it to be due to arrest of the heart. Oliver and Bolam[6] came to the conclusion that currents of 200 volts act directly on the heart (*i. e.*, not through the vagal mechanism), but do not affect the respirations; with stronger currents, on the other hand, the heart and respiratory centre are simultaneously affected. Most of these workers further observed that the effect of the current and its lethality varies considerably for different groups of animals. Cunningham[7] concluded that fibrillary contraction of the heart was the usual cause of death.

Prevost and Battelli found that alternating currents of low tension (about 130 volts) cause only temporary arrest of respiration, but that fibrillary contraction of the ventricle is induced exactly similar to that which follows the application of a faradic current directly to the heart. In dogs these fibrillations always persist after the current is broken, so that, once the fibrillations have appeared, it is impossible to resuscitate the animal. In guinea-pigs and rabbits the fibrillations may sometimes disappear and the animal recover; whereas, in rats this latter result was invariably noted, this animal being apparently absolutely immune to low-tension currents. With very high-tension currents (1300 to 4800 volts), Prevost and Battelli[8] found that fibrillation of the ventricle does not occur, but rather that the beats become quicker and stronger, and that the arterial blood pressure rises. The respiratory centre, however, becomes paralyzed, and profound shock results. This respiratory paralysis could frequently be recovered from by the application of artificial respiration; and in dogs spontaneous reappearance of respiration was quite common. It was further noted that when the heart had come to a standstill—coincidently with respiratory cessation—massage of it brought on fibrillation. Still another most interesting observation deserves notice, namely, that the application of a high-tension current to a heart already in fibrillary contraction causes

[1] These observations were concluded a year ago, but the publication was withheld in the hope of our being able to prosecute the investigation farther. This we find now to be impossible.

[2] Prevost and Battelli. Loc. cit., No. 1.

[3] Der Tod durch Electricität, Leipzig, 1896.

[4] Death from Electrical Currents, New York Medical Journal, 1890, vol. lv.

[5] Prevost and Battelli. Loc. cit., No. 1.

[6] On the Cause of Death by Electric Shock, British Medical Journal, 1898, p. 132.

[7] A Text-book of Legal Medicine and Toxicology, Philadelphia, 1903, p. 261.

[8] Loc. cit., No. 2.

the fibrillations to disappear and the normal heart-beat to be re-established.

The other papers of Provost and Battelli refer to continuous currents (No. 3) and to the influence of the number of periods of the alternating current on its physiological effect.[1] In this latter research it was found that with very frequent alternating currents—*e. g.*, 1720 periods per second, a much higher voltage is necessary to produce death than when currents of low frequency (*e. g.*, from 9 to 150 periods) are used. It is also pointed out in this paper that the respirations, suspended during the application of the current, spontaneously reappear when the current is broken, provided the heart be not paralyzed. The other papers published in 1899[2] refer to the physiological effect of electrical discharges from condensers. Since these papers, others have appeared by Arloing,[3] Bordier et Lecomte,[4] and Guilnard,[5] but as there is nothing in any of these regarding the effect of alternating currents on dogs, a further reference to them will be unnecessary here.

Practically all the experiments carried out by us were with alternating currents, as used for illuminating purposes. In strength these varied between 400 and 2700 volts; in frequency sixty periods per second. In all cases dogs, rendered anæsthetic by morphine and A. C. E. mixture, were employed. The electrodes were made of copper or zinc, shaped either as thick rods, which could be placed in the rectum and mouth, or spoon-shaped, to apply to the surface of the body. The electrodes were usually wrapped around with a sponge soaked in saline solution, so as to increase the conductivity. The carotid blood pressure was recorded in most cases, and the respirations carefully observed.

The results of the experiments are summarized in the appended tables:

[1] Prevost and Battelli. Loc. cit., No. 4.

[2] Loc. cit., Nos. 5 and 6.

[3] Contribution a la connaisance de l'action des currents électriques continus a haut voltage sur les chevaux, Journ. de physiol. et de path. génér., 1902, tome iv. p. 976.

[4] Effets de l'application directe des courants de haut frequence sur les animaux, ibid., 1903, tome v. p. 564.

[5] Contributionàl étude des effets mortels produits par les courants électriques, ibid., p. 368.

No.	Strength of current (volts).	Position of electrodes.	Duration of application.	Behavior (general) of heart and blood-pressure.	Behavior of respirations.	Lethal effect.	Remarks.
1	2300	Mouth and rectum.	5 sec.	Fall to abscissa.	Cessation.	Death.	Artificial respiration and massage of heart without effect; adrenalin intravenously.
2	1000	"	17 "	"	"	"	Artificial respiration and massage of heart without effect; adrenalin intravenously.
3	2300	"	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used as in 3a.
3a	2300	"	"	Fall to abscissa.	Cessation.	Death.	Artificial respiration and massage of no avail; adrenalin intravenously.
4	2300	"	15 sec.	"	"	"	1 mg. atropin sulphate injected previous to application of current.
5	2300	Back of head and hind limb.	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used in 5a to 5d.
5a	2300	"	"	Marked rise.	"	"	1 mg. atropin sulphate injected previous to application of current
5b	2300	"	1 sec.	"	"	"	
5c	2300	"	5 "	"	"	"	
5d	2300	"	20 "	Fall to abscissa.	Cessation.	Death.	
6	2300	"	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used in 6a to 6c.
6a	2300	"	4 sec.	Momentary inhibition, then rise.	"	"	
6b	2300	"	5 "	Momentary inhibition, then irregular heart action; became regular on massaging.	Cessation, but recovered by artificial respiration.	"	Artificial respiration and heart massage resulted in recovery of normal heart-beat and respirations; this is the only result of this nature that was obtained.
6c	4000	"	5 "	Fall to abscissa.	Cessation.	Death.	The resistance of the dog had been depress'd by previous applications.
7	2300	"	2 "	Inhibition, then rapid beat.	Cessation, then recovery.	Recovered.	
7a	2300	"	10 "	Temporary inhibition.	Cessation, then recovery.	"	1 mg. atropin sulphate given previous to application of current.
7b	2300	"	10 "	Fall to abscissa.	Cessation.	Death.	Tissues at point of application of electrodes burnt; heat rigor of abdominal muscles.
8	2300	"	3½"	Fall to abscissa.	"	"	1 mg. atropin intravenously before electrocution; artificial respiration, heart massage and adrenalin injection without effect; P. M., auricles beating, ventricles in diastole.
9	2300	Leg and mouth.	2 "	Fall to abscissa.	"	"	Same measures as in 8 adopted without effect.
10	2300	Not recorded.	3 "	No effect.	Unaffected.	Recovered.	5 mg. atropin intravenously before electrocution.
11	2300	Head and leg.	Instantaneous.	Momentary fall.	"	"	Both vagi cut.
11a	2300	"	4 sec.	Fall to abscissa.	Cessation.	Death.	3 mg. atropin injection four minutes before application of current. 2.5 amperes passed through body; artificial respiration, adrenalin injection, etc., without effect.

No.	Strength of current (volts).	Position of electrodes.	Duration of application.	Behavior (general) of heart and blood-pressure.	Behavior of respirations.	Lethal effect.	Remarks.
13	1500 1 ampere	Head and leg.	2 sec.	Fall to abscissa.	.....	Partial recovery.	Artificial respiration and heart massage caused partial recovery of heart-beat and respirations, and dog came partially out of anæsthetic; readministration of anæsthetic (ether) caused death.
14	400	Head and foot.	Instantaneous.	Momentary inhibition.	Temporary cessation.	Recovered.	5 mg. atropin injected after application of current.
14a	600	"	"	Fall to abscissa.	Cessation.	Death.	Marked fibrillary contraction of heart.
15	800	"	"	Momentary inhibition.	.....	Recovered.	6 mg. atropin injected previous to application of current.
15a	800	"	"	Momentary inhibition.	.....	"	
15b	2300	"	"	Fall to abscissa.	Cessation.	Death.	Heart in marked fibrillary contraction; direct massage increased this
16	1000	"	"	.....	.....	Recovered.	No tracing taken; dog allowed to recover from anæsthetic; was in every way normal next day.
17	600	"	"	.....	.....	Death.	Marked fibrillary contraction.
18	400	On isolated heart.	.....	Fibrillation	.....	.....	Heart perfused by Langendorff's method (see text, p. 422).
19	400	On heart in situ.	6 sec.	Fibrillation	.....	.....	Perfusion of heart after fibrillations had appeared of no effect (see text, p. 422).
20	2700	Hind leg and head.	4⅕ "	Inhibition.	Cessation.	Death.	Window in thorax; heart quickly excised and perfused by Langendorff's method; auricles began to beat and ventricles to show fibrillations with occasional beats.
21	1500	.....	Instantaneous.	No effect.	No effect.	.....	
22	1000	Head and leg.	"	Momentary inhibition.	.....	Recovered.	Window in thorax.
22a	1000	"	"	Inhibition, then fibrillation.	.....	Death.	
23	1000	"	"	Inhibition, then fibrillation.	.....	"	Massage of heart; perfusion through coronary arteries with oxygenated Locke's fluid, anelectrotonus had no effect on fibrillary contractions.

The most noteworthy points of interest are: Firstly, the variable strength of current necessary to cause death; and secondly, the effect of the current on the circulatory system. By the study of the latter a satisfactory explanation is, we think, obtained of the cause of death in all cases.

With regard to the strength of current necessary to cause death, it will be noticed that this depends largely on the position of the electrodes. With these in the mouth and rectum death occurred

after a momentary application of 1000 volts (No. 2[1]); whereas, when they were placed on the head and hind leg a current of 2300 volts, repeatedly applied for periods of from one to ten seconds, did not cause death (Nos. 5, 6, 7, and 10). Even when the currents were similarly applied (viz., to back of head and hind leg), however, currents of equal voltage had a variable lethal effect; thus, in several cases 2300 volts momentarily applied caused death (Nos. 9 and 15), and this was also induced in some by a much smaller voltage (Nos. 14 and 17). After we have considered the effect produced on the blood pressure, we will be in a position to offer a satisfactory explanation of this irregularity in lethal effect.

The effect on the blood pressure is very striking; at first there is often a slight rise, then a distinct fall to below the abscissa, and then, if the current be only of short duration, a rise again to above normal. If the current be of longer application, however, the blood pressure does not recover. The temporary rise at the moment of application is probably due to muscular contraction and perhaps vasoconstriction. The inhibition which follows is due, in some cases at least, to stimulation of the vagus mechanism, for it could be prevented in one case by the administration of atropin (No. 5). Even when atrophinized, however, or when both vagi were cut (No. 11), this inhibition, with subsequent recovery, was not infrequently noticed, and in all cases where a strong current was applied for long enough (five to ten seconds), permanent fall of the blood pressure was observed, even when the animal was deeply atropinized. Obviously, then, vagal inhibition of the heart has nothing to do with the permanent fall of the blood pressure. By a direct examination of the heart, the cause of this permanent fall of blood pressure was found to be fibrillary contraction of the ventricle, the auricles, meanwhile, continuing to beat normally (Nos. 8, 11, 14, 15, 18, 19, 20). By directly applying the electrodes to the heart, the mode of onset of this condition was more closely studied. It was found that when the current was closed, there was entire inhibition of the ventricle, and that when the current was broken the fibrillary twitchings started at the base. A current of one volt directly applied to the heart was sufficient to induce the fibrillation.

In one experiment we excised the heart and perfused it through the coronary arteries with defibrinated blood by Langendorff's method. When the beats had become normal a momentary current of 400 volts was applied to the base. The normal beat was immediately replaced by fibrillary twitchings, which persisted until the heart was quite dead.

In another experiment, after producing fibrillary twitchings with the heart *in situ*, it was quickly excised and perfused by Langendorff's method; in about two minutes normal contractions of the

[1] These numbers refer to the table.

ventricles reappeared at the rate of 90 beats per second, but the fibrillary twitchings still persited.

Direct massage of the heart *in situ* was also frequently attempted, but without avail. Anelectrotonus, produced by using various strengths of voltaic current, was likewise without effect on the condition.

We had not an opportunity of applying a very powerful and rapid alternating current, which is stated by Prevost and Battelli (loc. cit., No. 2) to arrest the fibrillation, nor did we cool the ventricle as practised by Porter[1] to dissipate the fibrillations produced by ligature of the coronary arteries. With the strongest current at our disposal (viz., 2700 volts, No. 20), applied for 4.5 seconds through electrodes placed on the head and hind limb, we noticed that the heart was merely inhibited, fibrillation not appearing until after the heart had been excised and massaged by hand, in point of time, eleven minutes after the current had been applied.

The respiratory movements were invariably brought to a standstill during the application of the current, on account of the tonic convulsions coincidently induced. They reappeared, however, when the current was broken, provided this was only of so short duration that no fibrillary contraction of the heart existed. Whenever fibrillary twitching had occurred, however, the respirations remained permanently inhibited, and this was true, even after vigorous artificial respiration.

The application of a current of 1000 volts for an instant through electrodes placed on the head and hind limb does not seem to permanently damage the nervous tissues, for in one dog (No. 16) in which this was done and the animal allowed to recover from the anæsthesia, no change from his normal behavior was perceptible (the reflexes were normal; there was no paralysis, etc.).

Coming now to the question of variability in the strength of current necessary to cause death, we are convinced that this depends on the path through the body traversed by the current.[2] If the heart lies in this path, fibrillary contractions will result; if not so, only vagal inhibition. Currents passing between electrodes in the mouth and rectum necessarily traverse the heart and are always fatal. With the electrodes on the head and hind limb, on the other hand, most of the current will pass along the tissue about the spinal column and will frequently pass by the heart.

In several experiments we placed the electrodes on the head and anterior extremities, and invariably noted vagal inhibition of the heart, general convulsions, and respiratory cessation, but no delirium cordis. The respirations returned, and the heart started beating when the current was broken.

[1] American Journal of Physiology, 1898; vol. 1. p. 71.

[2] This explanation was first brought forward by Tatum (loc. cit.), and Cunningham, A Textbook of Legal Medicine and Toxicology, Philadelphia, 1903, p. 247.

In other experiments we placed the electrodes on the two anterior extremities, with results similar to those obtained in the previous cases, except in one dog in which fibrillary contractions followed the application of a current of 2300 volts for about ten seconds. Some of the current in this case had undoubtedly spread to the heart.

These observations seem to us to suggest *a possible prophylactic measure* for workers exposed to the danger of strong currents; viz., that they should wear a corset made of some conducting material; for example, copper. This corset, to be of any value, would require to be closely applied to the skin about the shoulders and base of the neck above, and to the lower portion of the trunk below; and opposite the cardiac region it would require to be separated from the skin by some non-conducting material—for example, India-rubber. It would certainly be of no use merely to wear such a corset separated from the skin along all its length by woollens, as, we are told, has been practised.

We are greatly indebted to the Cleveland Electric Illuminating Company for supplying us with the necessary current, and to Mr. E. E. Noble, their superintendent, who manipulated the apparatus for us.

THE PHYSIOLOGICAL RELATIONSHIP OF THE PROTEIDS OF THE BLOOD PLASMA.

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of Philadelphia.

Although it is evident that there must be wide variations in the composition of the blood plasma even in health and that this variation must affect the proteid element of that fluid, still, owing to the great technical difficulties in the separation and estimation of these bodies, it is only within recent years that their study has been taken up vigorously, and so far the work on them has been almost entirely experimental, our knowledge of the subject not being sufficient to make it of clinical use. I was able to make the series of experiments on the variations of the proteids of the plasma under varying conditions, which form the basis of this paper, in the laboratory of Professor Franz Hofmeister, in Strasburg, whom I wish to thank for his constant help during the course of the investigations.

The separation of the proteids of the plasma was very inaccurate and unsatisfactory until the method of salting out was developed. This method is based on the fact that the addition of certain salts to solutions of proteids renders these insoluble. The various proteids of blood plasma are precipitated at different concentrations, and by adding varying amounts of certain salts at least four dis-

tinct bodies may be separated, viz: fibrinogen, euglobulin, pseudoglobulin, and serum albumin. The salts which are best adapted to the purpose are magnesium, ammonium, and sodium sulphates, and of these I selected the last, because it contains no nitrogen and all globulin is precipitated by half saturation, thus avoiding the necessity of adding dry salt. This salt reaches its highest solubility at 35° to 40° C., and therefore it is necessary to keep the solution constantly at this temperature and to do all filtering and other manipulations at the same. The sodium sulphate solution referred to in this article is one kept concentrated under these conditions.

These bodies after precipitation have previously been estimated by weighing of, or by determination of the nitrogen in, the precipitate. It seemed to me that it would be both easier and more accurate to determine the nitrogen in the filtrate and from this to calculate the amount in the precipitate, and my results have confirmed this opinion.

The method of preparing the body proteids from those of the food is still somewhat obscure, and it is uncertain whether each of the proteids of blood plasma arises independently or whether they are formed from a common mother substance—*e. g.*, serum albumin. The latter is made probable by the observation of Moll that serum albumin in the presence of sodium carbonate kept at a temperature of 56° C. for half an hour is partly converted into euglobulin and pseudoglobulin.

My experiments were performed with a view to throwing some light on this question.

We believed that if an animal were bled freely and then well fed, a comparison of blood drawn before and after the bleeding would show in the latter an increase of that proteid, if any, which stood nearest to the assimilation form. Also, that by starvation a relative decrease of the same form could be brought about.

The conduct of my experiments was as follows in all cases: The blood drawn by means of a glass cannula from an artery flowed directly into a measuring-glass which contained an amount of normal salt solution, plus 0.4 of sodium oxalate to prevent coagulation, equal in volume to the blood to be drawn. This mixture was immediately centrifugated and the clear plasma drawn off from the corpuscles. A specimen of this diluted plasma was measured off for nitrogen estimation; to a second specimen was added a quarter of its volume of sodium sulphate solution, to a third one-half, and to a fourth its own volume, a series of tests with gradually increasing amounts of sodium sulphate having shown that these concentrations lay between the limits of the globulins.

These mixtures were always made by adding the sodium sulphate solution to the plasma in a measuring-glass and filling up to a certain mark, thus avoiding contraction of the liquid. They were then poured into test-tubes which were stood in the same vessel of

water and kept at body temperature. The extractive nitrogen was estimated by further diluting the plasma with four times its volume of water and boiling. While boiling a few drops of a concentrated solution of zinc sulphate were added and the vessel removed from the flame. The solution of zinc sulphate is strongly acid and addition of too much, or prolonged boiling after addition, is likely to result in the formation of an acid albuminate. In such cases addition of sodium carbonate and boiling again has always given me a biuret free filtrate. The above precipitates were all filtered off and a measured amount of the filtrate taken for nitrogen determination.

All tests were carried out twice from the beginning, the precipitation being done separately and if the two did not agree well a third or fourth was made. In a few cases a control test was made with a much more dilute plasma and dilution was found to have no influence on the size of the precipitate.

The numbers obtained have been expressed as percentages of total proteid nitrogen. This avoids the disturbance from varying amounts of water in the plasma and shows better that in which we are especially interested, the relation between the different proteids.

Owing to the great variation in the percentage of globulin and especially of fibrinogen in different dogs, it is only possible to compare the results obtained from the same dog under varying conditions with each other. This makes a large series of bleedings necessary and limits the amount drawn each time to the least possible quantity.

In one of my last experiments I was surprised to find that although after standing at body temperature two hours there was a good precipitate of fibrinogen, after standing about five hours this had almost entirely disappeared. This was evidently the result of fibrinolysis, and the thought occurred to me that perhaps a partial process of the same nature might account for the very low numbers for fibrinogen which I have occasionally found. If this were so we would expect to find a large amount of albumin in the corresponding tests and this has always been the case. As the lysin would also be active in the euglobulin and pseudoglobulin precipitates, the small numbers for fibrinogen would not increase their apparent size. However, as this process is rather rare, it may generally be neglected.

1. Influence of Hemorrhage. The animals were bled freely at intervals of several days and the blood thus drawn used for examination. The tables show the amount drawn each time and the interval as well as the results obtained.

It will be seen that in the dogs an additional proteid appeared which seemed chemically to be a nucleoalbumin and which gave the plasma a turbid appearance. It was present from the first in the second dog but no cause for its presence could be seen. As this body is precipitated with the fibrinogen it increases the apparent

amount of that body and explains the increased amount found in the last column of the first series. A rough estimation of its amount showed that from 0.6 to 0.8 per cent. should be subtracted from the number given for fibrinogen. In the second dog it was more accurately determined.

EXPERIMENT I.—Dog, weight 7.2 kilograms.

	Date.				
	Nov. 23.	Nov. 26.	Nov. 30.	Dec. 7.	Dec. 14.
Cubic centimetres of blood drawn	145	72	80	108	75
Total nitrogen in 100 c.c. plasma	1.162	1.093	0.947	0.810	0.767
Fibrinogen (+nucleoalbumin)	17.7	10.7	9	16(9)	13.7(7)
Euglobulin	8.2	12.3	19	24	17.3
Pseudoglobulin	48.5	28	14.5	20	22.4
Albumin	25.6	49	57.5	40	46.6

EXPERIMENT II.—Dog, weight 3 kilograms.

	Date.			
	Feb. 17.	Feb. 22.	Feb. 24.	Feb. 26.
Cubic centimetres of blood drawn	150	75	75	75
Total nitrogen in 100 c.c. plasma	0.676	0.824	0.865	0.764
Nucleoalbumin	5.5	9	9.7	7
Fibrinogen	2.4(17.4)	14	7.3	6
Euglobulin	13.5	12	12.7	11
Pseudoglobulin	19.3	21	21.5	20
Albumin	59.3(44.3)	44	48.8	56

The first column here varies so widely from the normal that its value must be somewhat discounted, but if we suppose the presence of fibrinolysis and substract, say, 15 per cent. from the albumin and add it to the fibrinogen the series seems much like the one above.

EXPERIMENT III.—Rabbit, weight 1.5 kilograms.

	Date.			
	Feb. 5.	Feb. 9.	Feb. 15.	Feb. 19.
Cubic centimetres of blood drawn	30	30	30	30
Total nitrogen in 100 c.c. plasma	1.048	0.789	0.737	0.767
Fibrinogen	13	10.5	10	8.7
Euglobulin	16	7.5	11.5	11.5
Pseudoglobulin	11	18	14.5	18.3
Albumin	60	64	64	61.5

Burckhardt, determining the globulin by dialysis, found in rabbits an increase of total globulin after hemorrhage, a result which does not agree with mine, although his method was too inaccurate for his results to have any great value. The most striking change in the blood, which I have found, is the steady and rapid fall in the per cent. of fibrinogen, although the rise in the albumin was almost as marked, especially in the dogs.

2. INFLUENCE OF STARVATION. The dogs used for this experiment were first kept for two days without food and then placed on half the quantity of meat necessary to retain nitrogen equilibrium. After several weeks of such hunger they were given unlimited quan-

tities of meat or bread, the tables giving the quality and quantity of food. An error in the estimation of fibrinogen made it necessary to state this with the euglobulin.

EXPERIMENT IV.—Dog, weight 10 kilograms.

	Date.			
	Dec. 20.	Jan. 5.	Jan. 13.	Jan. 25.
Diet	Normal.	2 wks. ⅓ diet.	3 wks. ⅓ diet.	12 days meat freely.
Total nitrogen in 100 c.c plasma	0.784	0.702	0.946	0.868
Fibrinogen and euglobulin	18	41.5	32.5	38
Pseudoglobulin	26	15	26.5	21
Albumin	56	43.5	41	41

EXPERIMENT V.—Dog, weight 13 kilograms.

	Date.		
	Nov. 10.	Nov. 23.	Dec. 8.
Diet	1 wk. ⅓ diet.	3 wks. ⅓ diet.	2 wks. bread freely.
Total nitrogen in 100 c.c. plasma	1.454	1.240	1.184
Fibrinogen and euglobulin	45	52	21
Pseudoglobulin	22	14	13
Albumin	33	34	66

EXPERIMENT VI.—Dog, weight 8 kilograms.

	Date.	
	Nov. 23.	Dec. 8.
Diet	3 weeks ⅓ diet.	2 weeks meat freely.
Total nitrogen in 100 c.c. plasma	1.107	0.749
Fibrinogen and euglobulin	26	23.5
Pseudoglobulin	24	7.5
Albumin	50	69

The results of these experiments show in agreement with Burckhardt, Wallerstein, and Levinsky that the percentage of albumin is decreased during hunger, and that the greater part of the loss is made up by the fibrinogen and euglobulin, the pseudoglobulin being more irregular.

SUMMARY. One of the most striking facts shown in the tables is the wide variation in composition of the plasma in apparently normal dogs. This may be due to diet or to diseases which are not sufficiently severe to show themselves—*e. g.*, mild intoxications or infections. It seems, however, that there is an attempt to retain the percentage of total nitrogen at about the same figure and this shows much less variation than do the various proteid bodies.

The fact that after loss of blood the percentage of fibrinogen falls seems to show that this body is replaced with greater difficulty than any of the others, while the increase in albumin points to this as the first stage in metabolic formation of proteid. The globulins seem more irregular in behavior. This relation is also upheld by the relative decrease in albumin during hunger as this body would not be replaced from the food as rapidly as under normal conditions. This increase in globulin, as well as the appearance of nucleoalbumin after loss of blood, may, however, be due to the decrease

in total proteid in the plasma and the necessity of keeping it at about the same point, causing the withdrawal from the solid tissues of the body, of these proteids, in which they are especially rich.

It seems certain at least that albumin and fibrinogen do not arise in the same way and under the same circumstances, and the probability of the globulins being formed from serum albumin, either in the blood or elsewhere, perhaps by ferment action as Moll has proposed, is heightened by my results.

LITERATURE.

1. Burckhardt. Archiv. f. exp. Pathologie, Bd. xvi. p. 332.
2. Moll. Hofmeister's Beiträge, 1903, Bd. iv. p. 563.
3. Levinsky. Pflüger's Archiv, 1903, Bd. c. p. 611.
4. Vallerstein. Thesis, Strasburg, 1902.

THE INCIDENCE OF GASTRIC AND DUODENAL ULCER IN PHILADELPHIA.

WITH SPECIAL REFERENCE TO THE POST-MORTEM RECORDS OF THE PHILADELPHIA HOSPITAL.

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THE following figures from the analysis of the post-mortem records at Blockley (the Philadelphia Hospital) were undertaken at the request of Dr. Osler for Dr. C. P. Howard's paper on "The Incidence of Gastric Ulcer in America."[1] They were not, however, completed in time to be incorporated in that paper, so that I present them now as an additional side-light on this interesting subject. I entirely agree with Dr. Howard's statement that we cannot base accurate or conservative conclusions on data obtained from clinical observations, and for that reason have confined myself to autopsy records alone. The discrepancies in clinical figures are well illustrated in his paper, where he deals with the subject from that standpoint. To quote him: "The figures from Philadelphia are rather puzzling. The University Hospital returns, kindly furnished me by Dr. James Tyson, give 19 cases out of 3979 admissions, or 0.48 per cent. On the other hand, the Pennsylvania Hospital has a very much smaller percentage—*i. e.*, 0.13. This discrepancy cannot be accounted for by any apparent reason." (Unless one takes into consideration the acknowledged uncertainty of the diagnosis in many instances, and the wide opportunity this offers for clinical error.)

[1] Medical News, October 8, 1904.

"In Baltimore we meet with similarly anomalous figures. At the Johns Hopkins Hospital there have been only 70 cases of gastric ulcer out of 16,553 medical admissions for a period of about fifteen years. This gives a percentage of 0.42. which is below New York (0.44 per cent.), yet higher than Philadelphia (0.16 per cent.). But in striking contrast are the figures from St. Joseph's Hospital, Baltimore, giving 4 cases out of 3298 medical admissions, or only 0.12 per cent. This, then, gives for Baltimore a percentage of 0.37, very far below New York, and still farther below Montreal (0.92 per cent.), and Boston (1.28 per cent.). These figures are interesting, and, no doubt, in a sense, indicative of the relative frequency of gastric ulcer in the localities specified, but surely lacking in the accuracy of the post-mortem figures given subsequently in the same paper as follows:

CLINICAL PERCENTAGES.

City.	No. medical admissions.	No. gastric ulcers.	Per cent.
Boston,	33,506	432	1.28
Montreal,	20,466	189	0.92
New York,	31,690	138	0.44
Cleveland,	3,427	13	0.38
Baltimore,	19,831	74	0.37
Philadelphia,	43,709	72	0.16
Chicago,	3,930	6	0.15
Denver,	5,040	6	0.12
Total,	161,599	930	0.57

Breslau and Zurich	0.66 per ct.
London	0.78 "
Berlin	1.33 "
Edinburgh	2.02 "

AUTOPSY PERCENTAGES.

City.	No. autopsies.	No. gastric ulcers.	Per cent.
San Francisco,	551	13	2.35
Boston,	3,089	57	1.84
New York,	561	8	1.42
Philadelphia,	826	10	1.21
Montreal,	3,158	33	1.04
Cleveland,	433	4	0.92
Baltimore,	2,223	19	0.85
Total,	10,841	144	1.32

London	4.6 per ct.
Europe	8.54 "

The great difference in the total number of autopsies in the several cities strikes me as also being probably a source of fallacy in calculating the absolute and relative frequency of ulcer in the different localities. In some instances, notably in the case of San Francisco, New York, and Cleveland, they seem to me too small in the aggregate to base a fair average upon. All such figures are, however, distinctly valuable, and bear out Dr. Howard's conclusions—*i. e.*, "I. Both clinically and pathologically ulcer is less frequent in America than in London and on the Continent. 2. That both clinically and pathologically ulcer is more common in the northeastern than in the more southern regions of America, with the exception of San Francisco."

Militating against the view expressed above—*i. e.*, of using post-mortem records only, are the opinions of Mayo,[1] who thinks that acute gastric ulcer is by no means as rare as it is usually considered. He says that it must be recognized clinically, for it usually heals, and the treatment is purely medical. "It is

[1] Medical News, April 16, 1904.

altogether probable," he says, "that the vast majority of acute ulcers heal, but a considerable minority fail to do so and constitute a share of the chronic ulcers. A chronic ulcer is frequently, if not usually, chronic from its inception."

If it is true that the "vast majority" of acute ulcers heal, then the objections raised to the results of post-mortem study on this subject by Byron Bramwell should also be mentioned. He thinks that acute ulcers often leave no scars and are not discovered at autopsy, or the scars if present are slight and often overlooked, so that a certain number of ulcers are overlooked in post-mortem statistics. Admitting the likelihood of these fallacies in acute ulceration, I still consider autopsy records the much surer way of computing the absolute and relative frequency of gastric and duodenal ulcers, certainly of the chronic forms.

The generally accepted causes for gastric ulcer are anæmia, hyperchlorhydria, certain occupations like shoe-making and tailoring, mechanical injury, the grinding action of the pyloric end of the stomach (Mayo), chlorosis and menstrual disorders, embolism and thrombosis (Virchow), as in heart disease or continued vomiting, superficial burns, and lastly (and often rather casually mentioned), nephritis and tuberculosis. It will be seen from the statistics below that the great majority of these ulcers (which we must consider as the chronic forms) are associated with some chronic dyscrasic disease, as, for instance, nephritis or tuberculosis.

It will be seen in the accompanying cases that in almost if not quite every instance there was an associated condition (in 0.76 per cent. of the cases nephritis or tuberculosis), to which in some manner we must consider the ulcers, usually multiple, etiologically related. So that I feel these two factors, nephritis and tuberculosis, should be emphasized more emphatically in text-book descriptions of gastric ulcer than is usually done.

In this connection, it would be interesting if we knew more about the relation of the stomach to chronic nephritis. Very little investigation has been done in regard to the perversions of gastric function in this relation, though such perversions are relatively frequent in nephritis. The investigations of Biernacki[1] seem to show that the secretion of gastric juice is in general reduced in all cases of inflammation of the kidney. Occasionally hydrochloric acid was absent, especially in severe cases of nephritis, during the stage of œdema, while it was present in milder cases, in large or small quantities. The secretion of pepsin was reduced, even in mild cases, while the motor power of the stomach was frequently found increased, not only in mild cases, but also in old chronic cases. He thinks that the glandular function is inhibited by toxic metabolic products, and that organic changes take place in the stomach in those cases in which

[1] Centralbl. f. klin. Med., 1890, Berliner klin. Wochenschrift, 1891.

nephritis has persisted for a long time and in which the blood changes are considerable and the nutrition of all the tissues has suffered. It may well be that one of the results of this perversion of function is the chronic gastric ulcer.

Since the time of Cruveilhier[1] (1835), who first recognized this condition, there have been numerous and classical reports upon gastric and duodenal ulcer, both in France and Germany. Rokitansky[2] (1839) and Jaksch[3] (1843) published careful studies in relation to gastric ulcer, while Krauss[4] (1865), Chvostek[5] (1882), and Oppenheimer,[6] (1891) have done the same in relation to duodenal ulcer. Indeed, following Cruveilhier's description, there have been in Europe, particularly Germany, an almost continuous series of experimental studies and reports contributing to our knowledge of these interesting morbid conditions. The foreign literature upon the subject is now enormous.

This has not, however, been the case in America, and accurate figures gleaned from autopsy records, while slowly making their appearance, as in Dr. Howard's valuable paper, are still all too scanty. So that any data, however inconsiderable, should, I feel, be welcome to those interested in scientific medicine.

LIST OF PATIENTS ADMITTED TO MEDICAL DEPARTMENT OF THE PHILADELPHIA HOSPITAL (BLOCKLEY) FROM JANUARY 1, 1893, TO DECEMBER 31, 1902 (INCLUSIVE).

(Vols. 16, 17, 18, 19, 115½, 116.)

Men's Medical Ward,			1893 . . .	1524	
"	"	"	1894 . . .	1506	
"	"	"	1895 . . .	1568	
"	"	"	1896 . . .	1475	
"	"	"	1897 . . .	1254	
					7327

(Vols. 116, 126, 127, 128, 133, 152, 153.)

Men's Medical Ward,			1898 . . .	1358	
"	"	"	1899 . . .	1899	
"	"	"	1900 . . .	1545	
"	"	"	1901 . . .	2013	
"	"	"	1902 . . .	1809	
					8,124
			End of ten years		15,451

(Vols. 124, 125.)

Men's Alcoholic,			1893	517	
"	"		1894	468	
"	"		1895	396	
"	"		1896	497	
"	"		1897	515	
					2385

(Vols. 124, 125, 157.)

Men's Alcoholic,			1898	720	
"	"		1899	710	
"	"		1900	1002	
"	"		1901	978	
"	"		1902	989	
					4399
			End of ten years		6784

(Vol. 120.)

Men's Detention,			1893	369	
"	"		1894	338	
"	"		1895	395	
"	"		1896	363	
"	"		1897	368	
					1833

(Vol. 154.)

Men's Detention,			1898	386	
"	"		1899	424	
"	"		1900	508	
"	"		1901	574	
"	"		1902	502	
					2394
			End of ten years		4227

[1] Anatomie Pathologique, 1829–1835, vol. i.; Revue médicale, 1838; Arch. gén. de méd., 1855.
[2] Oestreich, Jahrb., 1839.
[3] Prague Vierteljahrsschr., 1843.
[4] Das perforirende Geschwür in Deutsch, Berlin, 1865.
[5] Wien. med. Jahrb., 1883.
[6] Mang. Diss. Wurzburg, 1891.

(Vol. 123.)				(Vol. 155.)			
Men's, Colored,	1893	162		Men's, Colored,	1898	192	
" "	1894	149		" "	1899	183	
" "	1895	193		" "	1900	182	
" "	1896	201		" "	1901	279	
" "	1897	183		" "	1902	289	
			888				1125
				End of ten years			2013

(Vols. 66, 66½, 106, 113.)				(Vols. 113, 136, 139.)			
Women's Medical,	1893	468		Women's Medical,	1898	562	
" "	1894	562		" "	1899	621	
" "	1895	588		" "	1900	699	
" "	1896	536		" "	1901	784	
" "	1897	475		" "	1902	680	
			2629				3296
				End of ten years			5925

(Vols. 82, 111.)				(Vol. 139.)			
Women's Detention and Drunk,	1893	313		Women's Detention and Drunk,	1898	424	
" " " "	1894	331		" " " "	1899	436	
" " " "	1895	350		" " " "	1900	558	
" " " "	1896	343		" " " "	1901	553	
" " " "	1897	349		" " " "	1902	606	
			1686				2577
				End of ten years			4263
Women's, Colored,	1893	56		Women's, Colored,	1898	96	
" "	1894	62		" "	1899	92	
" "	1895	76		" "	1900	101	
" "	1896	83		" "	1901	116	
" "	1897	70		" "	1902	127	
			347				532
				End of ten years			879

Making a grand total of 39,542 cases in ten years.

Cases of gastric or duodenal ulcer coming to autopsy during this time:

1. (Vol. vi., p. 241.) Ulcer in duodenum, ½ cm. in diameter, with thick white edges; 8 cm. from pylorus; tuberculous ulceration of intestine; male, white, aged thirty-five years.

2. (Vol. vi., p. 244.) Small healed ulcer in stomach over pylorus, with a deposit of pigment, ½ cm. in diameter; interstitial nephritis and fatty heart; male, white, aged thirty-two years.

3. (Vol. vi., p. 262.) Along lesser curvature there are several small superficial ulcers in stomach; tuberculous ulcers in œsophagus and intestines; tuberculosis of both lungs; male, black, aged twenty-three years.

Vol. vi., from January 1, 1893, contains 53 autopsies.

4. (Vol. vii., p. 29.) Stomach shows scars of old ulcers; interstitial nephritis; female, white, aged fifty-five years.

5. (Vol. vii., p. 53.) Stomach shows a few very small ulcers; tuberculosis of lungs and intestines; male, black, aged eleven years.

6. (Vol. vii., p. 108.) Stomach shows not less than a dozen bodies in the mucous membrane resembling tubercles, which have under-

gone ulceration; miliary tuberculosis; male, white, aged thirty-two years.

7. (Vol. vii., p. 183.) Duodenum shows minute swelling and ulceration of solitary glands and at some points hemorrhage; miliary tuberculosis of right lung; parenchymatous nephritis; male, white, aged fifty-three years.

8. (Vol. vii., p. 203.) Cup-shaped ulcer of pyloric end of stomach; chronic parenchymatous nephritis; female, black, aged forty-two years.

9. (Vol. vii., p. 269.) At the pylorus and within the valve there is an ulcer on the lesser curvature and anterior surface about one and one-half inches in diameter; carcinoma of stomach, liver, lymph glands; female, white, aged thirty-seven years.

10. (Vol. vii., p. 270.) Numerous small ulcers in the stomach, toward the pyloric end, and also in the duodenum; hypertrophy and dilatation of heart; male, white, aged sixty-four years.

Vol. vii. contains 286 autopsies.

11. (Vol. viii., p. 60.) About 5 cm. from pylorus and on greater curvature there are some small ulcers about 2 cm. in diameter; miliary tuberculosis; male, black, aged twenty-three years.

12. (Vol. viii., p. 93.) There is an old cicatrix on lesser curvature, midway between œsophageal and cardiac orifices; interstitial nephritis; atheroma; female, white, aged fifty-six years.

13. (Vol. viii., p. 101.) There is a small ulcer in stomach; interstitial nephritis; female, white, aged forty-four years.

14. (Vol. viii., p. 274.) A healed ulcer in posterior wall of stomach, 10 cm. from lesser curvature and 5 cm. above pylorus; scirrhus carcinoma of pylorus; female, white, aged fifty years.

Vol. viii. contains 297 autopsies.

15. (Vol. ix., p. 8.) Stomach contains three small ulcers, round and clear cut; one, 9 mm. in diameter on anterior surface near pylorus, perforating; a similar one at other extremity on median and posterior aspect, and a third on the interior surface, 4 cm. from last one, 11 mm. in diameter; chronic bronchitis; chronic gastritis; male, white, aged fifty-eight years.

16. (Vol. ix., p. 123.) Upon posterior surface of stomach, just above pyloric opening, there is a large perforating ulcer with raised indurated edges; carcinoma of stomach; male, white, aged fifty-four years.

17. (Vol. ix., p. 259.) There are multiple round ulcers in stomach and duodenum; perforating ulcer of duodenum; atelectasis of left lung; male, white, aged twenty-seven years.

18. (Vol. ix., p. 278.) There is a large ulcer in stomach a little behind and below pyloric orifice; interstitial nephritis; male, black, aged fifty-five years.

Vol. ix. contains 297 autopsies.

19. (Vol. x., p. 16.) There are ulcers in stomach varying in size

from a pinhead to a pea; miliary tuberculosis; male, white, aged sixty-three years.

20. (Vol. x., p. 92.) Duodenum is ulcerated; interstitial nephritis; female, white, aged sixty-seven years.

21. (Vol. x., p. 147.) On greater curvature there is a circular ulcer, 1 cm. by ¾ cm.; it is in posterior wall nearer to cardiac than to pyloric end, and is crater-like, with indurated edges; tuberculosis of lungs; chronic nephritis; female, white, aged twenty-seven years.

22. (Vol. x., p. 219.) There is a small, round ulcer, with well-defined margins, in greater curvature of stomach; parenchymatous nephritis; myocarditis and endocarditis; female, black, aged twenty-one years.

Vol. x. contains 311 autopsies.

23. (Vol. xi., p. 144.) On lesser curvature, on anterior aspect of stomach, there is a round ulcer, 1 cm. in diameter, which has nearly perforated; parenchymatous nephritis; gangrene of lungs; male, white, aged twenty-five years.

24. (Vol. xi., p. 286.) There is a small, round, superficial ulcer in stomach; gangrenous stomatitis; diphtheritic gastroenteritis; female, white, aged ten months.

25. (Vol. xi., p. 295). There is a small ulcer in the duodenum; enterocolitis; female, white, aged three years.

Vol. xi. contains 310 autopsies.

26. (Vol xii., p. 55.) Near the cardiac end in relation to the lesser curvature there is an ulcer which measures ½ cm. in diameter, is cup-shaped, with slightly indurated edges; lobar pneumonia; female, black, aged twenty months.

27. (Vol. xii., p. 154.) On anterior surface near pylorus is an ulcer, 2 mm. by 3 mm., with irregular undetermined base; miliary tuberculosis; extensive superficial burns, eight to ten weeks old; chronic parenchymatous nephritis; female, white, aged thirty-eight years.

28. (Vol. xii., p. 176.) In neighborhood of fundus and extending toward greater curvature there are large ulcerations; the largest of these is probably 9 cm. to 10 cm. long and 8 cm. to 10 cm. wide; the ulcers tend to surround the cardiac end; the edges are ulcerated and thickened; tuberculosis of lungs; male, white, aged forty-eight years.

29. (Vol. xii., p. 262.) About 10 cm. from pyloric orifice in greater curvature there is a small, clear-cut ulcer, about 12 mm. in diameter; base clean, edges sharp cut; tuberculosis of lungs; acute nephritis; male, black, aged forty-seven years.

Vol. xii. contains 300 autopsies.

30. (Vol. xiii., p. 10.) On posterior wall about six inches from pylorus is a peptic ulcer about the size of a quarter of a dollar; chronic interstitial nephritis; female, white, aged seventy-six years.

31. (Vol. xiii., p. 19.) Stomach contains a few peptic ulcers of small size; chronic interstitial nephritis; male, white, aged sixty-eight years.

32. (Vol. xiii., p. 151.) Greater curvature shows a series of fine linear ulcerations arranged around œsophageal opening; these ulcers are about 4 mm. to 6 mm. in width; similar small ulcers are found in other parts of stomach; great anæmia; chronic nephritis; female, black, aged sixty-eight years.

33. (Vol. xiii., p. 169.) 6½ cm. from pylorus in anterior wall a large irregular oval ulcer is found, 5 cm. in length, opening in the long axis of the stomach; two more ulcerations, similar in character, but smaller, are noted; fatty degeneration of liver and kidneys; male, white, aged twenty-six years.

34. (Vol xiii., p. 220.) 5 cm. from pylorus is a loss of substance, 1 cm. to 2 cm. in diameter; base of ulcer is smooth; edges ulcerated and sharply cut; arteriosclerosis; chronic nephritis; female, white, aged sixty years.

35. (Vol. xiii., p. 170.) Within 5 cm. of pylorus are four small ulcers, varying from 1 cm. to 2 cm. in diameter, with elevated edges; chronic nephritis; fatty degeneration of liver; female, black, aged fifty years.

36. (Vol. xiii., p. 185.) Pylorus is occupied by pigmented tuberculous ulceration, oval in form, 4 cm. to 5 cm. by 2 cm. in extent; base, granular; tuberculosis; female, white, aged seventy-four years.

37. (Vol. xiii., p. 267.) Along lesser curvature, within 5 cm. of pylorus, is found an area of ulceration, 4 cm. in diameter, borders elevated and indurated; base of ulcer is bile-stained; chronic nephritis; male, white, aged seventy-four years.

Vol. xiii. contains 302 autopsies.

38. (Vol. xiv., p. 1.) Stomach contains a large tuberculous ulcer as big as a quarter of a dollar, not far from pylorus; miliary tuberculosis; male, black, aged thirty-six years.

39. (Vol. xiv., p. 71.) Stomach is the seat of a chronic catarrhal inflammation, with ulceration and thickening of its walls; tuberculosis; chronic nephritis; female, white, aged sixty-one years.

40. (Vol. xiv., p. 234.) There are several small ulcers in stomach, the largest is about 1 cm. in diameter; interstitial nephritis; male, white, aged fifty-five years.

Vol. xiv. contains 300 autopsies.

41. (Vol. xv., p. 129.) There are superficial depressions in the mucous membrane of stomach, which may be healed ulcers; carcinoma of uterus; female, white, aged fifty-seven years.

42. (Vol. xv., p. 213.) About midway between cardia and pylorus are two or three small ulcers, the largest is about 8 mm. in diameter; they are shallow, with irregularly raised margins; miliary tuberculosis; female, white, aged thirty-one years.

Vol. xv. contains 297 autopsies.

Vol. xvi., up to January 1, 1903, contains 77 autopsies. No case of ulcer of either stomach or duodenum to date.

Total number of autopsies in ten years, 2830.

CONCLUSIONS. The following grouping shows the ulcers in relation to their apparent cause. Those in association with:

Chronic Nephritis. (2) 6.244; (4) 7.29; (8) 7.203; (12) 8.93; (13) 8.101; (18) 9.278; (20) 10.92; (22) 10.219; (23) 11.144; (30) 13.10; (31) 13.19; (32) 13.151; (33) 13.169; (34) 13.220; (35) 13.170; (37) 13.267; (40) 14.234. Total, 17; 16 gastric; 1 ((20) 10.92) duodenal.

Tuberculosis, Miliary, or of Lungs. (1) 6.241; (3) 6.262; (5) 7.53; (6) 7.108; (7) 7.183; (11) 8.60; (19) 10.16; (28) 12.176; (29) 12.262; (36) 13.185; (38) 14.1; (42) 15.213. Total, 12; 11 gastric; I (7.183) duodenal.

Both Tuberculosis and Nephritis. (21) 10.147; (27) 12.154; (39) 14.71. Total, 3 gastric.

Chronic Bronchitis. (15) 9.8; gastric.

Pneumonia. (26) 12.55; gastric.

Atelectasis of Lung. (17) 9.259; both gastric and duodenal.

Carcinoma of Stomach or Elsewhere. (9) 7.269; (14) 8.274; (16) 9.123; (41) 15.129; Total, 4; all gastric.

Heart, Fatty. (10) 7.270; both gastric and duodenal.

Enterocolitis in Infants. (24) 10.286; (25) 10.295; both gastric. (Extensive superficial burns, with tuberculosis and nephritis. (27) 12.154. Classified above under Tuberculosis and Nephritis.)

Grand total, 42; total gastric, 38; total duodenal, 2; both gastric and duodenal, 2.

In 20 out of 42 cases, or 47 per cent., the ulcers were multiple. Mayo says that in 20 per cent. of cases more than one ulcer is present. Brinton,[1] in 463 autopsies upon cases with ulcer of the stomach, found 57 with two ulcers, 16 with three or four, 2 with five, and 4 with more than five.

The sexes in the above series were equally divided, there being 21 males and 21 females, and the average age for the males was forty-three years, and for the females the same, a remarkably equal distribution. Welch, in his statistics, found 40 per cent. in males and 60 per cent. in females. The largest number of cases in his series occurred in males between thirty and forty years, and in females between twenty and thirty years, but there was much uniformity in the distribution in relation to the four decades. In my series the greatest number of cases occurred in males, 5, between fifty and sixty years, and in females, 5, between forty and fifty years. Here, too, there was a tolerable uniformity in relation to the four decades. Three of the cases were in infants, ten, twenty, and thirty-six months old, respectively. Dr. Osler mentions a case reported by Goodhart in an infant thirty hours old.

[1] Ulcer of Stomach, 1837.

It should be borne in mind in relation to these figures that the age given is the age of death and not the age of the incidence of the ulcer, which must be considered as occurring earlier.

In regard to size, Dr. Osler mentions an ulcer 19 cm. by 10 cm., reported by Peabody, as the largest one he knows of. The largest one in my series (No. 28) was 9 cm. to 10 cm. by 8 cm. to 10 cm. The same authority refers to a case reported by Berthold in which there were 34 small ulcers. Similar cases of multiple ulcers are seen in my cases Nos. 10 and 32 above.

It should be remembered in basing conclusions on the above figures that the lame, the halt, and the blind of the city's streets sooner or later find their way to the Philadelphia Hospital and Almshouse, and that it is pre-eminently the house of chronic invalidism and disease.

Dr. Joseph Walsh, late pathologist to the Henry Phipps Institute, tells me that during his term of service (1903) he made autopsies on 52 cases dying of tuberculosis of the lungs, and that in one case there were numerous small superficial ulcers in the stomach. Dr. Rosenberger, who followed him, says that during the year 1904 there were 55 autopsies, and no instance of gastric or duodenal ulceration.

To briefly recapitulate, the total number of medical admissions to the Philadelphia Hospital for ten years from January 1, 1893, to December 31, 1902, inclusive, was 39,542. The total number of autopsies was 2830. The total number of ulcers was 42, of which 2 were purely duodenal.

So that the summary, including the figures given by Dr. Howard for the Pennsylvania and University Hospitals, is as follows:

Hospitals.	Number of autopsies.	Number of gastric ulcers.	Percentage.
Philadelphia Hospital	2830	40	1.41
Pennsylvania "	547	7	1.28
University "	279	3	1.07
Phipps Institute	107	1	0.94
City of Philadelphia	3763	51	3.15

REPORT OF FIFTY CASES OF APPENDICITIS AND FIFTY CASES OF HERNIA WITH REFERENCE TO ALBUMINURIA.

By F. E. Bunts, M.D.,
of Cleveland, Ohio.

In a paper read by Dr. John C. Munro before the American Surgical Association, in 1893, he calls attention to the significance of albumin and casts in surgical patients. It is particularly of interest

to note that he states that approximately 35 per cent. of all patients treated in the surgical ward showed signs of renal trouble. In concluding his paper he says: "We should expect evidence of renal irritation in over a third of the surgical cases found in a municipal hospital. The mere presence of a trace of albumin, with or without hyaline and granular casts, unattended by other evidence of renal damage, should not influence the prognosis in surgical disease or operation; and furthermore albumin and casts alone are apparently no contraindication to the administration of ether."

For some time my attention has been particularly drawn to the common occurrence of albumin and casts in the urine of appendicitis cases, so common, indeed, was this that I had been forced to feel that there was a definite relation between appendicitis and albuminuria and had in preparation a paper upon this subject. The statistics collected by Dr. Munro, however, made it appear that it was so common in all surgical cases that I concluded to take two classes of operations in which the peritoneum was opened, in one of which inflammatory processes were or had been present, and the other in which such was not the case. As a type of the first class I have taken 50 consecutive cases of appendicitis, and for the second class have selected 50 consecutive cases of hernia, none of which were the seat of inflammation.

These 100 cases may be summarized in the following manner: Appendicitis, 50 cases; of these, 43 were operated upon during the attack, and 7 between attacks, with 2 deaths. Examination of the urine showed albumin present in 18 cases previous to operation, disappearing after operation in 5 cases. Twenty patients who had previously been free from albuminuria developed it subsequent to the operation, making a total of 33, in whom it was present subsequent to operation.

Hernia (non-inflammatory), 50 cases; no deaths; of these, 11 showed albumin in the urine before operation, disappearing after operation in but 2 cases. Eleven new cases of albuminuria developed subsequent to operation, making a total of 20 in whom it was then present.

The number is obviously too small to have more than passing significance, and yet several interesting facts present themselves, and, should the collation of more numerous cases of a similar nature show similar results, might be of some value.

It may be said that these cases, with two or three exceptions, occurred in my service at Charity Hospital, and the examinations of the urine were made by one of the resident staff, assigned to that duty for four months at a time, and all doubtful examinations were subject to the approval or disapproval of the resident pathologist.

Referring to the tables, we find that of the inflammatory cases, 18, or 36 per cent., had albumin before operation, while of the non-

inflammatory cases, but 22 per cent. had albumin; 13, or 26 per cent., of the former had it both before and after, and 18 of the latter were similarly affected. Of the former, the albumin disappeared in 28 per cent. after operation, while in the latter it disappeared in but 18 per cent.

These observations, if they show anything, would tend toward the belief that intraperitoneal inflammation increases the frequency of the appearance of albumin in the urine in about 18 per cent. of cases; that operations in this class of cases cause the development of albuminuria in 40 per cent. of new cases, and an improvement or disappearance of albuminuria in 10 per cent.

In the non-inflammatory class, operations are followed by the development of new cases of albuminuria in but 18 per cent., and of disappearance of albumin in but 4 per cent. The smaller percentage cured by operation in the latter group suggests that the presence of albumin in non-inflammatory cases is more liable to be a permanent condition than in inflammatory cases.

It is a somewhat startling fact that 66 per cent. of all inflammatory cases operated upon had albuminuria subsequently, and 60 per cent. of these did not have albumin previous to operation. There is also a very decided difference between the percentage of albuminuria cases in inflammatory and non-inflammatory cases, both before and after operation. The statistics are very meagre, but they suffice to emphasize the observations in the paper already alluded to, that albumin is found in a very large percentage of surgical cases; that it cannot be considered on any ground yet established that it is of itself a contraindication to operation, for in the 100 cases here reported there were only 2 deaths, both acute suppurative cases, and among the cases of recovery from operation was a woman seven months pregnant, with albumin and hyaline casts, who was subsequently delivered of a full-term healthy child.

Unfortunately, there has been no systematic record kept of the condition of the urine at the time patients have left the hospital, so that no data can be offered at present as to the disappearance or continuance of the albumin and casts, but from records kept in a few scattered cases, I am of the opinion that a large number of them ultimately show no trace of kidney disturbance where such disturbance could originally reasonably be ascribed to the changes brought about by the surgical disease for which they were operated. While most of these cases have been operated under ether anæsthesia, it is a well-known fact that chloroform anæsthesia is followed not infrequently by the appearance of albumin in the urine.

IS THE TRANSPLANTATION OF THE CORD NECESSARY IN THE RADICAL CURE OF INGUINAL HERNIA?[1]

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The chief indication for the transplantation of the cord in the operative cure of inguinal hernia is the formation of a new canal and new rings in proper relation to each other.

The passage of the testicle in embryonal life, and, as a result, the presence of the cord necessitates a communication between the abdominal cavity and the scrotum. In order to prevent the escape of the abdominal contents through this opening, Nature has made the passage-way obliquely through the muscular walls of the abdomen; that is, with a deep ring above and internal and the superficial opening below and external, and these connected by a canal that contains the cord, but the lumen of which is normally obliterated by the apposition of the anterior and posterior walls. This obliquity, or the indirectness of the inguinal canal, is, perhaps, the chief factor in preventing the more common occurrence of rupture. When, for any reason, the intra-abdominal pressure is increased, this pressure is exerted at a right angle to the long axis of the canal, and has a tendency to hold the two walls in still closer relation and so help to prevent the formation of a hernia (Fig.1). This same valve-like action is seen naturally in the prevention of the regurgitation of urine by the oblique insertion of the ureter into the bladder, and artifically in the prevention of leakage after gastrostomy, and again, by the diaphragm after enterorrhaphy. Were it not for the obliquity the pressure would be parallel to the long axis, and would cause a widening of the canal and its openings (Fig. 2).

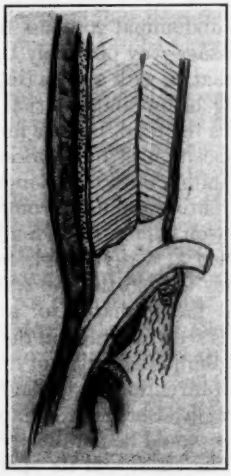
In practically all cases of inguinal hernia there is found to be a decrease in the obliquity of the canal and a widening of the rings, therefore, it has been reasoned that the radical cure will consist in the formation of new rings, and the construction of a new canal that will have the proper obliquity. This principle, including the transplantation of the cord, which we owe to the work of Marcy, Bassini, and Halsted, has been of the utmost importance in bringing the radical cure to that high standard upon which it now rests. Despite the improvements in the results that have followed these methods, there is still some dissatisfaction, as can be seen from the number of new or improved methods that have been submitted, for example, the method of Ferguson, which is based upon the relationship between the internal oblique muscle and the internal ring.

[1] Read at Colorado State Medical Association, Denver, October 6, 1904.

The deep or internal ring opens directly through the transversalis fascia, and under normal conditions is covered externally by the muscular structure of the internal oblique. With such circumstances, the attempt of any structure to pass through this ring will prove futile, because it will be forced back into the abdomen by the contraction of the internal oblique. In practically all hernias the internal oblique has been found to either completely or partially expose the internal ring, leaving the aponeurosis of the external oblique to counteract all increase of intra-abdominal pressure. Active contractile muscular tissue is certainly of more value in this respect than is fibrous tissue aponeurosis, even though this be distinctly attached to the muscle. Without this muscular check at the

FIG. 1.

FIG. 2.



a, skin; *b*, subcutaneous tissue; *c*, external oblique muscle; *d*, internal oblique muscle; *e*, peritoneum; *f*, transversalis fascia; *g*, transversalis muscle; *h*, cord.

very onset of an attempt to force a passage, the canal is much more liable to be made patent by a gentle and gradual insinuation of omentum or intestine at the internal ring. Many operators have found the lower border of the internal oblique above the internal ring, but the majority of them have considered this to be the result of the protusion of the sac; but Ferguson looks upon this malposition of the muscle as a congenitally deficient origin of the internal oblique from Poupart's ligament, and as such, a cause, and not an effect, of the rupture. This view seems to be well substantiated by dissections and experiments upon the cadaver, while operations for the radical cure, based upon this theory, seem to be eminently satisfactory.

The transplantation of the cord seems to be considered by many as an unnecessary and objectionable detail, and in recent work there may be noted a widespread disregard for the older teachings, with a tendency to avoid interfering with the cord, and in operating to attempt to repair and strengthen the anterior wall of the canal instead of making the posterior strong at the expense of the anterior.

After the general adoption of the Bassini type of operation, Wolfler, in 1892, was, perhaps, the first to suggest that a radical cure might be effected without a transplantation of the cord. E. W. Andrews, in 1895, suggested such an operation, but did not recommend it. In June, 1899, Ferguson presented his method, which he had performed sixty-four times in the previous eighteen months. At this time he was very positive, and enthusiastically recommended that the cord be left in its normal situation. He said: "Leave the cord alone, for it is the sacred highway along which travel vital elements indispensable to the perpetuity of our race."

Bloodgood, in the same year, in his classic work on hernia, in the *Johns Hopkins Bulletin*, mentions a number of cases in which he did not transplant the cord, and suggests that in certain cases the cord be left *in situ*, and in others that the veins alone be transplanted, leaving the vas deferens in its normal surroundings and attachments. He said that after the removal of the veins: "The cord is then such a small affair that it is a question in my mind whether it is necessary to transplant it."

In 1900 Girard, and in 1903 Hoffman, suggested methods similar, in that the cord is not transplanted. And in August, 1903, Halsted, of the Johns Hopkins Hospital, presented a method strikingly similar to some of the above mentioned. This list of similar operations, devised independently, for the most part, shows that a breaking away from the typical Bassini procedure is at hand.

The objections, more or less real, to the transplantation of the cord may be stated as follows:

1. *An interference with the circulation and the function of the testicle.* Orchitis and epididymitis have followed the Bassini type of operation in a certain number of instances, even hydrocele and varicocele have followed in such a manner as to lead to the supposition that the operation served as a causative factor. These points are well covered by the statistics of Bloodgood, which show them to be rare in the hands of experts, but the fact that they occasionally occur, makes plausible the supposition that their occurrence in other hands is more frequent. But that such sequelæ do take place will seem quite reasonable when it is remembered that the mesocord is separated from its attachments, the cord torn from its natural surroundings, and, after being roughly manipulated, for a longer or shorter time, is placed upon different structures, sometimes a row of foreign bodies, such as silver wire or other suture material. The cord is subjected to additional and unusual traumatism in its new

and comparatively unprotected location. The muscular structures that were normally in front have been placed behind, depriving it of their protection and at the same time forming a strong bulwark, which acts as a counterpressure for any force from the outside.

2. *Strengthening the posterior wall at the expense of the anterior.* The aim of the majority of operators and of all those who employ the Bassini method seems to be the construction of a new canal which will have an exceedingly strong floor or posterior wall. It would seem just as rational to devote the same or less time and trouble in repairing the natural canal and in making the anterior wall or roof exceptionally strong. The procedure in both instances will be about the same; the internal oblique and the transversalis are sutured to Poupart's ligament in the one in front and in the other behind the cord. A fact well worth considering and not to be overlooked in comparing these locations is that Nature placed the internal oblique in front of the cord.

3. *The complexity of the operation.* When compared with the new methods, those which transplant the cord will be found to be more complicated and time consuming; they also necessitate more handling, and again, in consequence, a greater possibility of infection.

4. *Recurrence.* Recurrences of the hernia follow the Bassini type of operation, but since improvements in technique, such as rubber gloves, improved absorbable suture material, and Coley's suture above the cord, the percentage has become so small as to be practically disregarded. Recurrences have also followed operation of the new form, but these have been comparatively few, and a proper estimate of the percentage cannot as yet be determined. Such accidents will follow each and every mode of operating in variable small percentages for apparent reasons that cannot be discussed under this title.

It will be readily admitted that these objections to the transplantation of the cord are of slight and insignificant importance when compared with the cure of hernia. The problem may be summed up in the question: Is it necessary for the accomplishment of a cure of hernia to subject the cord to such manipulation and dislocation that the functional integrity of the testicle may be threatened? If so, further consideration is practically unnecessary, for the great gain, the cure of hernia, will far outclass any small loss, such as a remote possible interference with the testicle. But, if answered in the negative, then it is certainly far better to leave the cord in its normal situation.

The operation for the radical cure of hernia without interfering with the cord may consist of the following steps:

1. Skin incision.

2. Incision of the aponeurosis of the external oblique, with an exposure of the canal.

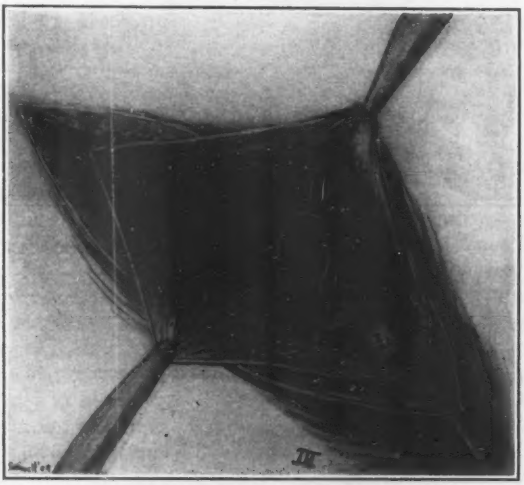
3. Dissection and removal of the sac, after the reduction of its contents.

4. Decreasing the size of the cord by the removal of the fat and veins if considered necessary. These steps are the same as in the usual operation for hernia.

5. Repair of the internal ring; the transversalis fascia may be brought together at the upper margin of the ring or the slack may be taken up below.

6. Suture of the internal oblique and the transversalis to the undershelving of Poupart's ligament for its outer two-thirds, as seen in Fig. 3.

FIG. 3.



7. Suture of the aponeurosis of the external oblique. This may be done by an ordinary suture, which, with the above steps, comprises the "Ferguson typic operation."

The imbrication, or overlapping of the aponeurosis, as suggested by E. W. Andrews, with different variations and modifications, has been employed quite extensively of late, and apparently with great satisfaction.

It has aided in the compilation of the latest so-called Halsted operation of the Johns Hopkins Hospital, and is quite generally employed, whether the cord is transplanted or not. The imbrication of the external oblique aponeurosis is shown in Figs. 4 and 5. Another method of introducing this stitch, as shown by Andrews in the presentation of his method, is one in which the transversalis, the internal oblique, and the upper flap of the aponeurosis of the external oblique are all included in the loop of the stitch. This has the advantage of applying but one row of sutures to Poupart's ligament.

8. Closure of the skin.

The writer's experience has been confined to thirty-two case in which the cord was not transplanted, and the internal oblique sutured to Poupart's ligament according to the Ferguson technique.

FIG. 4.

FIG. 5.

The external oblique was sutured in various ways. Of these, fourteen have been traced and heard from recently, two have had recurrence, but as one was complicated by an undescended testicle, and the other was operated upon for a recurrence after a Bassini operation, it would seem as though they would not serve as arguments against the method.

The object in presenting this short review of the subject is to submit it as a basis for a discussion of the question of the transplantation of the cord and to recommend the operation in which it is left *in situ*.

The great ease and simplicity, with the elimination of the danger of secondary changes in the testicle, are, perhaps, the more conspicuous reasons for its farther trial.

REPORT OF A CASE OF CHRONIC PYELITIS, DUE TO BACILLUS COLI COMMUNIS INFECTION, SIMULATING RENAL TUBERCULOSIS:

TREATED BY NEPHROTOMY, FOLLOWED BY THROUGH-AND-THROUGH ANTISEPTIC DOUCHES.[1]

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The following case is that of a woman coming to my service at St. Luke's Hospital, from the medical service of Dr. Evans, who presented a perfect clinical picture of renal tuberculosis. It illustrates to what extreme chronic infection of the kidney other than a tuberculous one may bring a patient.

The patient, Mrs. B., aged forty years, gave a negative family history. As a child she had had whooping-cough, but since then she had been free from contagious diseases. Has had a great deal of trouble, especially during the past few years, with her stomach and bowels. Her food digested poorly, giving rise to eructation, some pain, and occasional attacks of vomiting. Her bowels were persistently constipated. She had pain in the rectum and anus, giving rise recently to considerable distress. She had severe cystitis after the birth of her last child, five years ago. These symptoms recurred occasionally, and during the past two years have become at times very severe and troublesome. Her present illness dates back two years, during which time she lost strength and flesh. She has become continually worse since the beginning of the present year, complaining of pain in her right lumbar region, of almost constant difficulty and pain in micturition. She has been unable to digest any solid food for some time; has had numerous vomiting spells, almost constant distress and eructation of gas. During the past two weeks she has been unable to find anything which her stomach will tolerate. Previous to her admission to the hospital she has been having a temperature of 104° and over in the afternoon, according to the statement of her family physician, with sweating at night, and chilly sensations, though she has had no distinct chills.

On admission to the hospital the patient had a temperature of 99.4°, pulse of 80, respiration 18. During the five days of observation the temperature never rose above 100°. Examination on admis-

[1] Read before the San Francisco Academy of Medicine, July, 1904.

sion showed the patient to be very poorly nourished, very thin and emaciated, not much more than skin and bones. Heart and lungs negative. Marked tenderness over the whole of the abdomen, especially over the colon, most over the cæcum and sigmoid flexure. Epigastrium very sensitive. White blood count of 6600. She passed twenty-eight to thirty-six ounces of urine in twenty-four hours. It showed a specific gravity of 1014, acid, no sugar, faint cloud of albumin. Microscopically it contained a large amount of pus; no red blood cells. She was able to retain so little by mouth that rectal feeding was commenced. The urine was examined for the tubercle bacillus in vain. Fat was found in her stools to quite an extent. Five days after admission her ureters were catherized. Pus was found in the specimens from both sides, but by far the largest amount came down from the right side. This was again examined for the tubercle bacillus, but none found. This was not considered proof against renal tuberculosis, as this so often happens with very serious tuberculous lesions of the kidneys. Culture from this urine gave a pure culture of the bacillus coli communis. At the time I considered this a contamination, although every precaution had been taken to obtain a pure specimen. Guinea-pigs were injected, but the patient was considered to be in such a critical condition that the usual wait of six weeks was considered inadvisable. The diagnosis of a tuberculous infection of the kidney was made without any reserve, because of the clinical picture. A disordered stomach, accompanied by vomiting, painful and difficult micturition, a painful and enlarged right kidney, urine from the pelvis of the kidney containing large amounts of pus, and especially, and most important of all, a thin and emaciated individual, showing systemic inroads upon the vitality of the patient through a chronic period of two to three years, made the diagnosis seem positive to us. Therefore, an operation was advised and undertaken.

An enlarged and congested kidney was exposed, which, after proper protection to the surrounding tissues, was split from top to bottom into the pelvis. My surprise was great, I assure you, to find no abscesses or other evidence of tuberculous infection. A culture was made from the pelvis of the kidney, a drain passed from the pelvis through the wound and the kidney drawn together with three or four catgut sutures. Another drain was placed below the kidney, and the wound closed. The culture from the pelvis of the kidney showed another pure culture of the colon bacillus. The guinea-pig, which had been previously been inoculated, died in five days of general purulent peritonitis, showing the pure culture of the colon bacillus, which pretty fairly completed the diagnosis of chronic pyelitis due to the bacillus coli communis with general chronic toxæmia of the individual.

The patient, soon after the operation, developed successively an infection of each of the salivary glands, which subsided under the

influence of ice. Her general condition almost immediately began to improve. Her stomach settled, and she was soon able to be put upon a liberal diet, gaining as much as ten pounds a week. After the third day I irrigated right through into the bladder with formalin, 1:2000, and peroxide diluted one-third, for three and one-half weeks. On removal of the tubes, the wound healed almost in a night, and within a week nothing remained to be dressed. In seven weeks after operation she was on her feet, and walked out of the hospital on the fiftieth day.

The tenderness of the kidney, evidently due as much to congestion as to infection, gradually subsided; the bladder irritation disappeared and the amount of pus in the urine diminished to a very small quantity, possibly coming from the opposite kidney. A culture from the wound, one and a half weeks after the operation, showed colon bacilli still present, but none were found after the third week, which determined me in removing the tubes and allowing the wound to heal.

The interest in this case lies in the general systemic intoxication produced by this infection, and the rapid response of the system to the thorough douching of the pelvis of the kidney and ureters with the antiseptic solution. The indications for the nephrotomy were clear, and the great benefit derived from the through-and-through flushing of the infected tract, according to well-founded surgical principles, bespeaks for this radical method a more frequent application.

GUNSHOT WOUNDS OF THE URETER; TWO CASES OF URETEROVESICAL ANASTOMOSIS.[1]

By George Tully Vaughan, M.D.,

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Gunshot wounds of the ureter are so exceedingly rare that I feel it to be my duty to report the case which fell under my care. In the history of surgery, so far as I have been able to ascertain, there has been recorded only one authenticated case of gunshot wound of the ureter, and that was the case of the archbishop of Paris, who was shot June 29, 1848. The ball entered the right lumbar region close to the spine. There was great depression, pale, anxious countenance, nausea, vomiting, intense pain in back and in the course of the sciatic nerves, and paralysis of the lower limbs. Urine flowed from the wound in great quantities and there was none in the bladder. An attempt to remove the ball was made

[1] Read at the Thirteenth Session of the Association of Military Surgeons of the United States.

without success and death occurred eighteen hours after the injury. A necropsy showed that the ball had passed through the third lumbar vertebra dividing the cauda equina just below its origin and the left ureter close to the pelvis of the kidney and lodged in the psoas muscle.

The doubtful case of Rayer reported by Hennen seems to have been a gunshot wound of the kidney. My case was as follows:

CASE I.—C. T., colored, male, aged thirty years, laborer, was admitted to the Emergency Hospital on account of an abdominal fistula which had followed a gunshot wound of the abdomen received October 3, 1903. The ball, a 0.32, entered about one inch to the inner side of the right anterior superior spinous process of the ilium and just below Poupart's ligament and lodged under the skin behind in the median line, having perforated or notched the fourth bone of the sacrum, whence it was removed.

A purulent discharge with symptoms of peritonitis followed and on October 11, my colleague, Dr. W. P. Carr, suspecting perforation of the bladder or bowel did an exploratory laparotomy in the median line. Numerous adhesions were found but no wound of the abdominal viscera. The wound was closed, with drainage in front, and in a week there was a purulent discharge in front through the opening for drainage and behind at the point of exit of the bullet, so daily through-and-through irrigation was used. The patient gradually improved, the discharge became thinner and looked almost as clear as water. On examination it was found to contain a little pus and a trace of urea. December 3, 1903, the patient was discharged recovered, with the exception of the fistula in front.

He was readmitted March 15, 1904 for the purpose of getting cured of the fistula, which had continued to discharge since leaving the hospital and kept his clothing constantly wet. A slight discharge also came from the posterior wound. The patient suffered no pain, ate and slept well, was well nourished and able to work. He voided from the bladder about 22 ounces of urine in twenty-four hours and from the fistula, judging from the amount collected for several hours, by means of a tube in the fistula, 2 ounces an hour or 48 ounces in twenty-four hours.

Examination of urine from the bladder gave the following result: reaction, acid; specific gravity, 1022; urea, 6 grains to the ounce; no albumin or sugar; a few pus cells. Fluid from the fistula appeared thin and slightly milky in color, reaction faintly acid; specific gravity, 1010; urea 1 grain to the ounce; pus cells abundant; a trace of albumin present. A probe could be passed into the fistula in front to the depth of four and three-quarters inches when it was arrested by a hard body, probably bone. Through the posterior opening the probe could be inserted to a distance of a little over two inches.

A diagnosis of wound of the right ureter was made and on March 19th the patient was operated on. The abdomen was opened along the outer border of the right rectus muscle and afterward the rectus was divided transversely just below the navel. The probe inserted through the anterior fistula was used as a guide but the operation was tedious and difficult on account of the numerous and strong adhesions of the intestines with one another and with the pelvic walls. The right ureter was finally exposed. It was found dilated to at least twice its normal size and was traced into a mass of unusually dense adhesions in the bottom of the pelvis. In attempting to free the ureter it was broken off at the location of the fistula as was shown by the appearance of the proximal end.

Nature was making a brave attempt to close the fistula, and incidentally the ureter itself, as at the site of the fistula the ureter was much contracted in calibre—being not larger than one-fourth or one-fifth of the dilated portion above. The result of this contraction was not only dilatation of the ureter but also probably damage to the kidney, as shown by the small percentage of urea found in the urine from the fistula. Sewing together the ends of the ureter (uretero-ureteral anastomosis) would have been almost impossible even if desirable, at this point, so ureterovesical anastomosis was decided upon. The bladder was opened in front and a small oblique opening was made through its posterior wall on the right side at a point considerably above the normal opening of the ureter. The end of the ureter was then split into two flaps about one-eighth of an inch long and drawn into the bladder by means of forceps introduced through the anterior and posterior openings. The flaps were spread open and stitched to the inside of the bladder by sutures whose knots were tied on the peritoneal surface of the bladder. The ureter was also sewed to the posterior surface of the bladder at its point of entrance. Very fine silk sutures were used. The anterior wound in the bladder was closed by two rows of continuous sutures—using first, catgut through all the coats, and second, silk, omitting the mucous coat and inverting the first row. The ends of the rectus muscle were united with heavy catgut, the longitudinal wound was closed with through-and-through silkworm-gut interrupted sutures and continuous catgut for the peritoneum and sheath of the rectus. No drainage for the peritoneal cavity, but a small piece of gauze was left projecting from the space in front of the bladder. A catheter was kept in the urethra several days to prevent distention of the bladder, but there was slight escape of urine from the anterior wound for a few days. The patient was discharged recovered April 19th. The urine was measured several times before the patient was discharged and was variable—running from 32 to 84 ounces in the twenty-four hours. April 17th Dr. F. R. Hagner reported as the result of a cystoscopic examination that the bladder mucosa was normal. The new open-

ing of the right ureter was seen as a small papillary mass from which urine flowed. A catheter was inserted into the old (normal) opening of the right ureter for about one and one-half inches beyond which it would not go. The scar in the front wall of the bladder was smooth.

The patient was again seen June 15th, about three months after the operation, when he appeared to be in perfect health.

CASE II. *Cancer of the rectum; inguinal colostomy; later excision of rectum and part of colon; right ureter divided; ureterovesical anastomosis.*—Mrs. E. T., white, aged forty-seven years; was operated on June 8, 1903, an inguinal colostomy being done on the left side, on account of ulceration of the rectum which had existed about a year and resisted all treatment. The patient's health improved after this operation and she gained in weight but continued to discharge pus and blood, so it was decided to remove the diseased rectum. March 14, 1904 this was done through the posterior wall of the vagina, but the disease was found to extend so high up the bowel, that the abdomen had to be opened and all of the rectum from just above the sphincter up to and including a portion of the sigmoid flexure was removed. In doing this the right ureter was accidentally severed near the bladder. The proximal end was split and sewed into the bladder exactly as in the former case.

There was no leakage so far as known either from ureter or bladder, and the patient made a good recovery and was discharged April 29, 1904.

Conservative surgery of the ureter may be said to date from the year 1877, when the first ureterovesical anastomosis was done by Tauffer. Previous to that time division of the ureter was usually treated by removal of the corresponding kidney, and even as late as 1893 we find Hermann Thompson stating that complete cure in lesions of the ureter is to be obtained only by removal of the kidney. He condemns grafting into the bladder or intestine as methods not to be recommended. Yet in the same year, sixteen years after Tauffer's case, we find the second successful ureterovesical anastomosis done by Novaro.

The next year, 1894, F. Westermark performed the operation under the impression that his was the first successful case in the human being. Since then the enormous increase in the amount of abdominal and especially pelvic surgery has provided numerous occasions for the operation so that by 1903 Bovée had collected 111 cases of ureterovesical anastomosis, with seven deaths.

This operation is indicated whenever the lower part of the ureter has been divided or resected and the proximal end is long enough to reach the bladder. I believe it is to be preferred to any of the methods of uretero-ureteral union which have been suggested or practised for the following reasons given by Baldy:

(1) It is much easier to perform; (2) it is less likely to be followed by stricture, and (3) in case a stricture does form it is more accessible and easier to treat.

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SCABIES IN THE UNITED STATES OF AMERICA AND CANADA.

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SCABIES is a disease assignable to the category of those which have been known since the earliest periods of antiquity. The contention that it is included with those designated under the title "Zaarath" in the Hebrew scriptures—a term which in the English translation of the Books of Kings and Leviticus has been rendered "leprosy"—is at least significant of a belief respecting its prevalence at an early period of the world's history. The literature which has accumulated on the subject of both the symptoms of its invasion of the human family and on the absurd errors which have been committed respecting its nature and effects is voluminous. Since the day when St. Hildegarde first unmistakably referred to the acarus as its effective cause, and Bonomo and Cestoni, in 1787, presented their detailed description of the itch-mite, traversing the epoch when Hahnemann set forth his doctrines respecting the existence of "internal itch," as far as the hither side of the middle of the last century, when even distinguished physicians in France still doubted its origin in the encroachments of an animal parasite, the essays which have multiplied on the theme have been well-nigh innumerable.

Once the exact nature of the disorder established, its literature naturally contracted within channels. Volume One, for example,

of the Index Medicus furnishes but nine references to this subject in the medical literature of the world in all languages for the year 1903. Selecting at random single copies of half a dozen of the best known dermatological journals of this century, there is in all but a single abstract devoted to the same title—published in the *British Journal of Dermatology* for the year 1901.

The recent and unmistakable increase in the number of cases of scabies occurring in this country must be the excuse for again directing attention to a well-worn subject. The countries of North America have never been to a considerable extent the breeding-grounds of the sarcoptes hominis, even though at times the subject of frequent and well-sustained efforts at its colonization. This will appear the more singular if it be remembered that at the present day many of the cities of the United States and Canada vie with the capitals of Europe in the size of their populations and in the unwholesome crowding together of the unwashed classes in sleeping quarters and tenements.

There remains, nevertheless, a wide discrepancy in the comparison. The extent of the overcrowding of population in the larger towns of Europe is well illustrated in the most populous of them all, the metropolis of London. In the year 1901 the British census disclosed the fact that on an area of 117 square miles in that city more than four and one-half millions of people were bestowed. In the city of New York, the largest of the New World, there were fewer than three and one-half millions of people, in the year 1900, confined to an area of 326 square miles. "Greater London," with an area of 691 square miles, provides shelter for more than six and one-half millions of residents; while "Greater New York," which includes the population of Westchester County in the same State, and Bergen, Essex, Hudson, and Union Counties in the State of New Jersey, held only a few more than four and one-half millions of people on an area of 1258 square miles.

In this connection it is interesting to note that in the year 1870 and those immediately following, attention was attracted to the very large number of persons living especially in the Northern and Western States of this country, who were reported to be extensively affected with an "itch" supposed to be scabies. In some of the smaller villages and towns of the region mentioned it was said that every inhabitant was affected with the disease in question; and this irrespective of sex, age, or social condition. The affection was denominated "prairie itch," "winter prurigo," "frost itch," "winter itch," "swamp itch," and other names suggestive either of the State in which the disease prevailed, or of the lumbermen's camps where it also flourished. All attempts failing to recognize an efficient parasite in the production of the symptoms, it was finally shown that the affection was produced by the climatic changes, occurring often with marked severity in the northwestern

part of the country, in the autumn and winter chiefly, aggravated by the coarse clothing worn by many of the people, as well as by the use of cheap soaps, and often of parasiticides employed to secure relief from a fancied infestation. The patients presented all the evidences of extensively developed cutaneous pruritus, some even exhibiting vesicular lesions in the interdigital spaces, the features, however, in other points not closely resembling those of scabies. It was exceedingly difficult at the outset to persuade both physicians and patients that these were not instances of the "itch" or a similar contagious disease. It was noticeable that the disorder prevailed in the country as well as in the city, and that every man, woman, and child in certain communities was reported to be affected, a proportion never observed even where scabies is extraordinarily prevalent. During these years scabies prevailed in the northwestern part of the United States in a proportion scarcely greater than between 2 and 3 per cent. of all existing dermatoses.

The fruitful and unfailing source of scabies in North America is Europe, and in particular the crowded capitals of the Old World. Statistics showing the prevalence of the disease on the other side of the Atlantic are not available. Estimates, however, may be based on the annual reports of the out-patient departments of hospitals in England, France, Germany, Austro-Hungary, the Netherlands, and Italy, making it seem probable that on the lowest computation 25,000 cases of scabies are treated yearly in the capitals of these countries. It will appear probable in what follows that the number of cases of this disease seen in all the larger cities of North America in one year does not equal the number treated annually either in Vienna or Berlin, to say nothing of the larger totals represented in the statistics of London, or, more particularly, Paris.

The conditions favoring an increased colonization of the acarus on this side of the Atlantic are well known. These conditions are twofold and often related. The first requires an unusual increase in immigration to this country of passengers for the most part arriving in the steerage of transatlantic vessels; the second requires an unusual stimulus to the crowding together of the native-born populations of this country. At times these two conditions coexist; in other years the one may be effective without the co-operating influence of the other. It is also true that in different years the one may have a preponderating influence over the other. Stimulants to the crowding together of the native-born population are recognized in the desire of the people of the country to travel from their homes to visit great fairs, such as those opened in Chicago, San Francisco, and St. Louis, as a result of which enormous aggregations of human beings are housed for a brief time within relatively restricted limits. The vast army which Xerxes marched to Sardis has been exceeded in numbers by the visitors to one of these fairs on a single day.

Other stimulants to an unusual and extensive massing together of certain classes of the population of this country are the demands created by war. Here the crowding together of individuals, chiefly of the male sex, results in personal contacts which, by reason of the necessities of military life, are both intimate and imperative. Every one who has given attention to the subject understands that the casual contacts of hand-shaking, and even of the physical examination of patients made by physicians and students of medicine, rarely suffice to transmit scabies from an infested to a sound individual. Those are efficient contacts which become possible during the occupation of a bed in common, or those required when two individuals are engaged in toil seated closely to each other and exchanging articles during the hours of labor, with hands frequently touching; or those, again, common between mother and child, and between children at play together. These afford opportunities for the transference not of a male acarus only, or even of a single female, but of numbers of the young of both sexes, which are thus placed in a favorable condition for multiplication and colonization.

One of the earliest opportunities for the spread of scabies in North America was furnished by the exigencies of the War of the Revolution. At this period, when accurate statistics of disease are not available, proofs of the prevalence of scabies are found in the letters of officers of the Continental army and of civilians. These bear evidence of the degree to which many suffered during the war and for a time after hostilities ceased. A striking illustration of the difference between the people of that day and of this is furnished by the merchants, who are always ready to profit by the needs of sufferers. Of all remedies vaunted in the advertisements of the press of the present day for the relief of pruritic affections of the integument, few, if any, for the relief of "the itch" are pressed upon the attention of the public. Yet the daily journals of the larger cities of this country, as well as the shelves of the apothecary, during and soon after the War of the Revolution, bore witness to the number of secret remedies and nostrums for the cure of scabies.

The knowledge had to-day on the subject of the prevalence of scabies in North America is practically limited to the statistics furnished by the American Dermatological Association, compiled by its Committee on Statistics and published in annual reports of the Association from the year 1878 to the present time. These data have been accorded scant credence, both by some of the members of that body and by others not counted in its ranks, and this chiefly, if not wholly, by reason of the insufficiency of the returns, an objection obviously well grounded. The statistics of the Association are assuredly not those representing the frequency of skin diseases throughout the entire country, and certainly do not give the actual number of cases occurring in the cities from which the reports are

forwarded. They none the less possess an especial value of their own as indexes of the larger totals existing but never tabulated, and they have been greatly esteemed by those who have had occasion to refer to them, for they are the statistics collated exclusively by experts, who have agreed to reject from their lists cases not coming under their personal observation. Not only so, but they are furnished by men to whom the members of the medical profession not engaged in special practice have been pleased to send patients not falling within the lines of their own work. Further, they represent an experience in the largest cities of this country, and that an experience had in special hospitals and clinics, whither have resorted not merely patients afflicted with diseases of the skin, dwelling in such cities, but also those coming from adjacent smaller centres of population, many of whom, as is well known, naturally gravitate to the capitals where gratuitous aid is furnished. Lastly, with respect to the special affection here considered, it is well known that scabies, of all skin disorders, is most rife in populous centres, and probably occurs in a proportion of less than 2 per cent. of all dermatoses in the villages of the country. Exception, of course, is here made of the lumber- and mining-camps of the Northwest, and of the pseudo-towns which spring up in a day on the advance lines of a railway projection and which disappear as the iron parallels are pushed farther into a virgin territory.

The most serious flaw in the tables given below relates to the figures obtained from the city of New York, for in successive years represented in the compilation the returns from that city have not been made with equal fidelity and completeness. One of the reasons for this is to be found in the extreme difficulty of collecting the data from a large number of charities, widely separated in space the one from the other, many of them under different official management and with a non-coöperating staff. It is further to be noted respecting the tables appended that although the first statistics of skin disease ever collected in this country appear in the report of the committee published for the year 1878, no details are given in that year respecting scabies, the name not even appearing in the list. It will also be seen that the division of cases into public and private was not observed subsequent to the year 1887, the placing of all cases in one category after the date named being ordered by the Association in order to save contributors from the somewhat unpleasant necessity of reporting details giving a clew to the extent of their private practice. In the year 1891, further, it was determined that the statistical year should be changed from that extending from July 1st of one year to the thirtieth day of the ensuing June, to the twelve months represented in the calendar year. As a consequence, the figures for six months of the year 1891 are given, without itemization of the sources, at the foot of the column appended to the regular report.

The following table shows the number of cases of scabies reported from each of the cities named for each year of the period during which these statistics have been collated:

TABLE I.—CASES OF SCABIES REPORTED TO THE AMERICAN DERMATOLOGICAL ASSOCIATION.

Cities.	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889	1890
Montreal	.....	.....	.....	.....	.....	8	39	.....	92	.....	127	76	7
New York	.....	14	35	64	76	132	52	36	178	.....	151	282	87
Brooklyn	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Boston	.....	35	29	22	67	96	179	224	334	374	494	368	254
Philadelphia	.....	9	13	11	30	25	.....	44	78	137	210	202	37
Baltimore	.....	.....	9	6	6	2	.....	8	8	24	24	.....	.....
Washington	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Chicago	.....	18	14	31	22	72	56	56	34	72	59	80	48
Cleveland	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Cincinnati	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
St. Louis	.....	.....	.....	.....	1	7	13	74	.....	36	27	28	.....
New Orleans	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
San Francisco	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Buffalo	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Private	.....	15	15	7	26	34	33	49	56	62			
Public	.....	61	85	127	181	308	306	393	668	581			
Total	.....	76	100	134	207	342	339	442	724	643	1092	1036	433
Total No. of cases of skin dis. collated	.....	8117	11,047	11,076	11,514	15,838	9329	14,007	14,984	10,366	15,165	18,156	6807

Cities.	1891	1891	1892	1893	1894	1895	1896	1897	1898	1899	1900	1901	1902
Montreal	9	.....	20	8	20	16	9	20	17	.....	8	10	15
New York	31	.....	578	304	413	82	18	213	245	257	227	125	490
Brooklyn	.....	.....	.....	.....	59	32	35	89	60	70	31	29	.....
Boston	392	.....	189	278	242	133	130	156	67	129	136	153	485
Philadelphia	.....	.....	310	123	146	61	35	.....	.....	90	5	15	185
Baltimore	111	.....	.....	.....	.....	.....	.....	94	116	104	.....	.....	75
Washington	.....	.....	.....	.....	.....	.....	.....	.....	.....	42	32	37	27
Chicago	97	.....	84	127	46	32	31	42	23	27	34	30	80
Cleveland	.....	.....	10	35	44	9	13	10	18	23	16	47	34
Cincinnati	.....	.....	.....	.....	.....	.....	.....	.....	.....	31	49	33	43
St. Louis	47	.....	.....	26	29	18	.....	5	14	54	6	25	32
New Orleans	.....	.....	.....	.....	.....	.....	.....	36	17	27	24	46	.....
San Francisco	.....	.....	.....	.....	.....	.....	.....	.....	20	.....	.....	21	19
Buffalo	.....	.....	.....	.....	.....	.....	.....	.....	.....	30	.....	.....	.....
Total	687	985	1191	901	999	383	266	615	583	897	568	373	1345
Total No. of cases of skin dis. collated	13,038	17,784	25,797	19,272	24,821	15,130	10,880	23,925	21,973	31,280	22,455	21,976	32,462

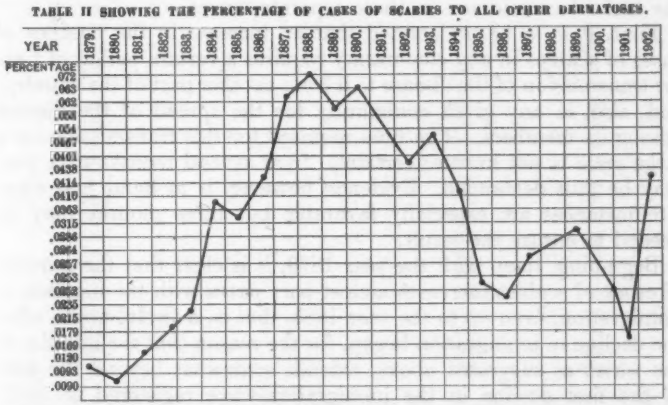
The total number of dermatoses collated in the statistics of the American Dermatological Association from the year 1878 to the year 1903, inclusive, is more than 440,000 (up to the year 1903 the figures were 439,552). This represents a population greater than that of either Washington, D. C., San Francisco, New Orleans, or Milwaukee, and is nearly that of Cincinnati and Los Angeles

combined, the figures being those taken from the last census. The total number of cases of scabies reported is about 16,000 (the figures at the last report, inclusive, were 15,526). This represents a population larger than that of Baton Rouge, La., or Annapolis, Md., and is very nearly that of the city of Rome, N. Y. For the entire period the proportion of scabies to all other dermatoses recognized in the Association lists is about 3 per cent.

In consulting the table it should be remembered that in successive years not only was the experience of each reporter enlarging, but the population also of the country, including that of the cities from which the returns were made, was furnishing a progressively larger area for observation. As time went on, the Association had occasion to enlarge its list of contributors by additions from several cities not represented in the earlier days of its organization.

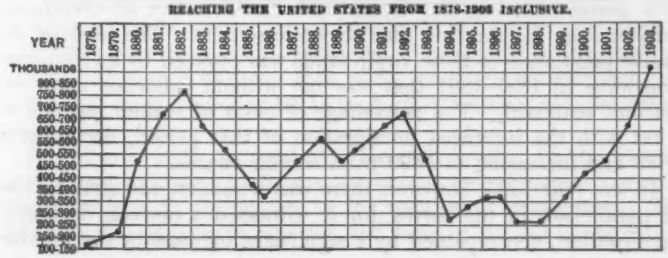
The following table represents the percentage of cases of scabies to each total number of cases of diseases of the skin reported for each separate year:

TABLE II SHOWING THE PERCENTAGE OF CASES OF SCABIES TO ALL OTHER DERMATOSES.



For the purpose of comparison, the following table is appended showing the number of immigrants arriving in this country from all others for each of the years named:

TABLE III SHOWING THE NUMBER OF IMMIGRANTS FROM ALL COUNTRIES REACHING THE UNITED STATES FROM 1878-1903 INCLUSIVE.



The first impression received from an examination of these tables suggests a relation to economic questions not pertinent to the subject under consideration. For example, the columns indicate with tolerable clearness the improvement of the social condition of our people following the resumption of specie payments in the year 1879, an improvement that continued for several years that followed; they point to a financial prosperity of the country at large, preceding the disastrous period between the years 1892 and 1896; they indicate a reduction in the number of immigrants when the Spanish War of 1898 doubtless withheld many from adventuring to a new land; and they significantly explain an enormous increase in the number of foreigners seeking these shores during the last three years of unparalleled prosperity.

If, however, one should expect to find the rise and fall in the scabies list correspond exactly with that of immigration, the result would be disappointment. A somewhat deeper insight into the significance of the facts throws light upon both the coincidence and the lack of coincidence in these separate waves.

First, it is to be understood that an increase in the number of cases of scabies in any community requires a certain period of time for transmission of the disease to it from another part of the country; and, also, in any given community for the spread of the disease among its members. The time required for this transmission on a large scale is not known; certainly, from several months to a year may be thus demanded. Evidence, however, is at hand that when circumstances are especially favorable but three months may be needed to ensure the result.

Beginning, then, with the year 1879, it is clear that the number of cases of scabies increases almost *pari passu* with the increase in immigration, even up to the year 1883, that is, a twelvemonth after the decline in immigration began, for the reason that the impulse of the wave, as suggested above, extends somewhat beyond the date of the first decline in the immigration-wave registered in 1882. The decline in the scabies wave, however, is distinct, as might have been anticipated, in the following year, viz., 1884, and doubtless resulted from the falling off in the number of steerage passengers reaching these shores at that time. The year 1888–1889 saw six new States added to the Union and the Territory of Oklahoma thrown open for the first time to white settlers. The push of the native population to these virgin lands was pursued by an immigration-wave in 1891–1892 that was not without influence upon the Eastern seaboard. The percentage of cases of scabies rose somewhat with the increased immigration of that period, declining in 1889 and increasing in 1890 from similar causes.

In the year 1893, however, there was a sudden and striking loss of parallelism in the waves, for it witnessed a marked decline in immigration, accompanied by a significant increase in the number

of cases of scabies reported. This was, without question, due to the crowds of native population flocking to the World's Fair in the city of Chicago. Naturally, the influence of this wholly unprecedented massing of the people in a Western State had an influence upon the scabies statistics not so fully perceived in the Eastern cities, which theretofore had enjoyed the unenviable and almost exclusive privilege of supplying the West with colonies of acari. In the following table the statistical returns for the year of the Chicago Fair of a group of Western cities are contrasted with the same from the cities of the East. The figures speak for themselves:

TABLE IV.—CASES OF SCABIES REPORTED TO THE AMERICAN DERMATOLOGICAL ASSOCIATION FROM EASTERN AND WESTERN CITIES.

Year.	Eastern Cities.	Western Cities.
1878	.....	.....
1879	58	18
1880	86	14
1881	103	31
1882	179	23
1883	263	79
1884	270	69
1885	312	130
1886	690	34
1887	535	108
1888	1006	86
1889	928	103
1890	385	48
1891	543	144
1892	1097	94
1893	713	188
1894	880	119
1895	324	59
1896	222	44
1897	522	98
1898	505	92
1899	692	192
1900	439	129
1901	369	202
1902	1177	158

The table indicates clearly that in the year 1888, the year of the addition of the new States and of the opening up of the new Territory, more cases of scabies were reported from Eastern cities than in any previous year, the number being nearly double that reported for the preceding twelvemonth; while for the year of the World's Fair, in Chicago, there was an actual falling off, 384 cases fewer than in 1892, the year preceding; while the Western cities reported an increase of nearly 100 over that of the previous twelvemonth, the number of cases exceeding by 44 the highest number ever previously reported by them.

In the year 1898 occurred the war with Spain. In the autumn of that year and during 1899 the number of cases of scabies increased coincidently with an increase in the number of immigrants. The Western cities promptly reported 100 cases of scabies above that of

the previous year, the total number being within four of that representing the increase during the World's Fair. The increase in the number of cases reported from the Eastern cities was precisely 87.

Having in view the supposedly careful examination of immigrants made under the direction of the General Government in the city of New York, where most of the immigrants to this country are landed, on *a priori* grounds it might be thought that the published reports of the Commissioner-General of Immigration would throw light upon the question considered in these pages. But the result is disappointing. The published report, for example, for the year 1903 (the last issued) indicates that but seven immigrants during the year were scabrous, a figure manifestly erroneous as to the fact. It is possible that the inspectors of immigrants are engrossed with more serious problems than those which concern the animal parasites. Every incoming steerage passenger is not stripped and physically examined, as are applicants for admission to a well-ordered hospital. It probably suffices the inspector if the patient be free from symptoms of tuberculosis or other of the graver forms of disease which it is sought to exclude. Lepers have passed immigration inspection not merely in this country when coming, but also when returning after a trip homeward. Not many years ago, a leprous patient from Sweden, with the evidences of his ailment written so broadly on his countenance that two experts who examined him pronounced without hesitation on his condition, twice passed successfully what is popularly supposed to be an efficient barrier erected by the vigilance of the inspectors. Is it not subject for wonder that numbers of cases of scabies annually traverse these barriers without detection or hindrance? But it would be indeed a subject for wonder if the number of cases of scabies occurring in immigrants to this country during one year examined in the city of New York, was actually only seven as officially reported.

The year 1904 recently concluded furnished the amplest opportunity for the spread of scabies in this country which the acarus family has hitherto enjoyed. Briefly, there was, first, the largest immigration this country has ever received from abroad; and, second, a great fair held in the city of St. Louis, collecting in unprecedented numbers in a single district of Missouri the native-born population of the country, if not from all, at least from a very large number of all the States of the Union. Judging from the data collected in past years, the number of cases of scabies in this country should soon exceed that ever before recognized in its history. Such will assuredly prove to be the fact. The statistical report of the American Dermatological Association for the year 1903 will soon be published. The tables include returns from twelve cities of the United States and Canada, showing that a total of 1743 cases of scabies has been recorded, a figure exceeding by 348 the largest number ever previously reported for one year from the same

sources. These are indications of the general spread of the disorder which are not without special significance.

For the first time in many years, scabies is developing in private practice. Between fifteen and twenty years ago, it was rare indeed that a case of "the itch" in this country occurred in the well-to-do classes of society consulting their family physician for relief of their ailments. If there is to be an unusual extension of scabies from the conjunction of the two co-operating causes cited above, the result should have begun to be apparent after about the middle of the summer, when most of the visitors to the Fair had had time to return to their homes and when the newly-arrived immigrants had had sufficient opportunity to distribute their uninvited guests in the communities where they concluded to settle. During the year 1904, my associates and I were applied to for relief of no fewer than 48 cases of scabies in private practice, the larger number between August and the last of December. Our clinical cases for the same year numbered 150, not a very large figure for the out-patient department of a clinic in a large city. But when it is noted that one-third of all the patients applied for relief during the last two months of the year, it will be seen that the number of cases under observation is beginning to indicate the operation of the agencies alleged to be effective.

It has been said, not without some basis of fact, that in this country soap is too cheap and water too abundant to permit of great extension of scabies in any region for any length of time. The truth is, that while there have been recognized here a few instances of the severe form of disease still described under the title of "Scabies Norvegica" (somewhat misleading for the reason that typical forms of extensive scabies as originally thus designated have occurred in the Northwest) a different type of "the itch" is now prevalent. This is confusing to practitioners who have been made familiar in a past experience with instances either of severe non-parasitic pruritus cutaneus, or of the old-time forms of scabies illustrated in the colored plates which are in the hands of so many members of the profession.

In these illustrations of the disease, as also in the well-marked features presented by patients whom American physicians studying abroad have seen in attendance upon the clinics of the capitals of Europe, the symptoms are so pronounced as to be practically unmistakable. The hands, for example, are usually tumid and well sprinkled with commingled vesicopustules, papules, crusts, scratch-marks, and the characteristic burrows of female parasites. Elsewhere the classical regions of involvement between the two parallels furnished above by the line traversing the nipples and below by that passing above the upper border of the patellæ, furnish a picture similar to that presented in the two hands, though often the evidences of scratching, with resultant excoriations and crusts, blood-

stained from the induced oozing, are exaggerated. The subjective distress, of which complaint is commonly loud, is considerable.

Now, the symptoms of this disease, as they occur in private practice, especially, and at this date when the disease is spreading even among the cleanly and well-to-do classes are those modified by the habits of the patients of this class with respect to the bath and the clothing. As to the latter, while it is true that no evidence is at hand showing that the itch-mites infest the clothing of patients (in some cities, such as Boston, the clothing of scabies patients is subjected to hot-air treatment for destruction of parasites; in others as in Paris, no such precautions are taken), still, among the cleanly, when the disease has once developed, soft and unirritating underclothing contributes greatly to the comfort of the sufferer. It will be remembered that the class of people to whom reference is here made includes those occupying their own homes, those accustomed to the daily tub, those comfortably clad, those scrupulously careful as to the person, those who often may well be described as given over to frenzied anxiety respecting contamination and filth accumulation.

When persons of this class, actually victims of scabies, confront the practitioner (with the classical types of that disease formulated in his mind), an error is almost inevitable on account of the character of the symptoms in evidence. All the interdigital spaces carefully searched reveal possibly but two or three faint lines, scarcely suggestive of a well-excavated cuniculus. Elsewhere the axillary regions, possibly of both sides, often of but one (the left, where the predominantly used right hand finds easier accessibility to the skin) present two or three ill-defined, faintly discolored, flattish macules or papules. In the case of male patients, even those best washed, one can generally find at least a single papulopustule involving the skin of the penis or (more rarely) the scrotum, a practically pathognomonic symptom when considered in connection with others presented. Women occasionally have a similar lesion about the nipple or around the umbilicus. In these cases the complaint of nocturnal distress is fully as eloquent as in others with more classical symptoms of the disease. The patients, it should be remembered, are wholly unaccustomed to the incursions of bugs, fleas, and lice, and they highly resent the species of bodily torment to which they are subjected. In the case of mothers and of children, a history of contagion or of involvement of other members of the family can often be obtained.

The incautious practitioner, viewing the symptoms as far removed from those of the disease which represents scabies to his educated mind, is inclined to believe that they are produced by commoner causes of pruritus ("uric acid," harshness of climate, "defective metabolism," etc.); but no relief will be secured before the treatment is directed to removal of the efficient cause. He is more dis-

posed to err in these by-ways of difficulty for the reason, as before explained in these pages, that in America scabies in private practice up to a recent date was practically unknown.

If the details to which attention is here directed point to any definite conclusions, they portend no general and formidable extension of the pest in this country. The number of sufferers both in private and public practice will gradually increase beyond any limit heretofore recorded, and then there will follow the usual diminution in the number of the infested until the figures of the average of years are reached. Then the tidal wave will return when the country is again buffeted by a huge billow of immigration or agitated by some cause which determines a large movement of population within its borders. Whether the ultimate opening of the Isthmian Canal, which is to be practically a water-way of the United States of America, will exert a similar influence it may be too early to decide. But the important practical lessons of the situation are sufficiently obvious.

Ex uno disce omnes. The significance of the facts related concerns more than one of the serious problems of public hygiene. However large the rewards of international commerce from the point of view of economics, certainly at the present day the price to be paid involves the health and comfort of the people. The virgin territory of the United States of America has been bombarded for two centuries, from the North, from the South, from the far East, and from the distant West, with intermittent volleys of germs of leprosy, yellow fever, bubonic plague, Asiatic cholera, and the less deadly missiles furnished by colonies of animal parasites. These all are advance corps of the great army of Diseases of the Filth. The physical welfare of the people of this country demands practical measures for their safeguarding, but none the less a national education, which shall demonstrate the necessities of the House Cleanly before those of the House Beautiful.

X-RAY TREATMENT OF CUTANEOUS EPITHELIOMA.

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Among the factors to be considered in estimating the value of the *x*-ray treatment of cutaneous epithelioma, the most important is the liability to recurrence, and it is in this very particular that our knowledge is most limited. The purpose of this paper is to add something to the recorded data bearing on this subject. The cases are taken from the private practice of Dr. L. Duncan Bulkley, to whom I am indebted for the privilege of reporting them. The

diagnosis was always clinical. Biopsies are generally difficult to obtain, and in many of the cases, moreover, would be equivalent to excision, and subject to the same objections as the latter.

Before giving the clinical histories, however, there are two minor points of technique which I would emphasize.

1. The distance between the tube and the lesion should be made as short as is consistent with the avoidance of sparking from the apparatus to the patient. In treating a large area, like an extensive psoriasis, this rule does not hold. With a small lesion, as is usually the case in epithelioma, it reduces the time of exposure very materially; for since the quantity of rays received on a given surface varies inversely as the square of the distance between that surface and the anode, it follows that an exposure of four minutes at four inches is equivalent to one of twenty-five minutes at ten inches.

2. The screen used to protect the normal parts need not be entirely opaque to the *x*-rays. I have used ordinary rubber sheeting, folded into three layers, and have repeatedly carried the treatment to the production of a moist dermatitis of the exposed area, while the parts covered by the shield remained entirely unaffected. This seems to show that the rays which affect the skin have very little power of penetration. The advantages of this material are the ease of manipulation and the avoidance of the disagreeable tingling so often noticed when lead is used.

CASE I.—Female, aged forty-one years. The disease began about the year 1890 as a small pimple on the left temple. This was burned a number of times but the disease progressed, and in January, 1903, the whole left temporal region was covered with scar tissue, with a number of pearly nodules and small crusted areas scattered over it. At the outer extremity of the left eyebrow there was a triangular ulcer about a quarter of an inch on a side, with hard, raised edges. Between January 12 and March 27, 1903, the lesion received twenty-seven treatments, aggregating two hours and five minutes. The reaction was never carried beyond redness and scaling, but the ulcer healed, and the crusted and pearly nodules all disappeared, leaving a smooth, pale scar. On September 6, 1904, the patient wrote that there was still no sign of recurrence.

CASE II.—Male, aged seventy-eight years. The disease appeared first in 1891 as a small pimple in front of the lower end of the right ear. It was treated with some caustic, but recurred and was removed by operation in 1898. There has been no recurrence at this site, but in 1900 a small, scaling nodule appeared in front of the left ear. This second lesion was treated with mild ointments, and alternately healed and recurred, still gradually increasing in size, until October, 1902, when there was a small epitheliomatous ulcer with a slightly bleeding base. This healed after a single exposure of five minutes, but recurred, and in May, 1903, the treatment was renewed. The raw surface healed over readily, and

in July there was only one suspiciously red, slightly elevated nodule. Four months later this ulcerated, and then formed a crust, which fell and was renewed from time to time, but in May, 1904, it was still only one-eighth of an inch in diameter. Above it was a group of small, pearly, non-ulcerated nodules. Three exposures produced only a slight redness, but removed both lesions, except for a very thin crust on the lower. Even this crust disappeared within a month, and on September 19, 1904, the skin was perfectly smooth and soft, and showed no trace of a recurrence.

CASE III.—Male, aged fifty-nine years. In February, 1903, the patient first noticed a small, firm nodule in the left lower eyelid, near the border. It gradually increased in size and ulcerated, but without pain. On September 12, 1903, there was an ulcer about a quarter of an inch long by an eighth of an inch broad with a clean, moist base, and a firm, raised, perpendicular border. *x*-ray treatment was then begun, and by November 10 the ulcer was entirely healed. On December 9 a small, pearly nodule was visible, about a quarter of an inch external to the old scar, and the treatment was resumed, and continued with biweekly intervals up to January 28, 1904, when the induration was scarcely perceptible. The patient wrote on September 16, 1904, that there was then no trouble at the eye.

CASE IV.—Male, aged seventy-six years. The patient noticed several scaly patches on the face for about four years, and for the last six months a spot on the right malar eminence, on which a crust formed from time to time, occasionally falling and leaving a lightly bleeding surface. This lesion gradually extended upward, leaving a clear surface below, and at the beginning of treatment, March 20, 1904, was three-quarters of an inch in diameter, and covered with an adherent crust. There was no abnormal sensation save itching. One exposure of eight minutes was given, the anode being three and one-half inches from the skin. On May 9 the lesion had entirely disappeared, leaving a smooth, slightly red surface. The patient reported by letter, September 8, 1904, that the cheek was then well.

CASE V.—Male, aged sixty-one years. A pimple appeared on the left side of the patient's nose about 1895, and gradually spread into a broad superficial crusted patch. It was diagnosed as lupus erythematosus, and treated with local applications, with but slight improvement. Many flat seborrhœal warts developed on the face and hands, and in March, 1902, one of these, on the left malar eminence, became distinctly epitheliomatous. It advanced steadily until in October it had become a deep ulcer about three-quarters of an inch in diameter, with hard raised edges. Between October 21 and December 1, 1902, it was exposed to the *x*-rays sixteen times, aggregating ninety-seven minutes. This produced a moist dermatitis, which subsided in about three weeks, in which time

the ulcer was replaced by a smooth soft scar. The patient had occasional *x*-ray treatments later, but very irregularly. When last seen, on December 23, 1903, there was no trace of a recurrence of the epithelioma, and the area which had been inflamed by the active treatment was free from warts, while on the rest of the face these were quite numerous, though they always improved temporarily under mild *x*-ray treatment. The patient's niece wrote, September 12, 1904, that his face was well, except for a small spot on his nose and a very small place on his right cheek, which are presumably part of the old warty condition.

CASE VI.—Female, aged seventy-six years. For two or three years the patient had a small crusted spot about an inch below the left eye. She picked off the crust from time to time, but in September, 1902, it became adherent and bled a little when rubbed. There was a little itching occasionally, but no other sensation. Then for about a year she tried various mild ointments, but without improvement, and when the *x*-ray treatment was begun there was a hard, elevated, crescentic border about one-eighth of an inch wide and three-eighths of an inch long, with a shallow ulcer below it. Between September 18 and October 20, 1903, it received eight *x*-ray exposures, aggregating forty-three minutes. This made the skin very red and tender and produced some scaling, but the dermatitis subsided quickly, and by November 28 the skin appeared normal. On September 8, 1904, her son reported that there was still no sign of return, and that the scar was scarcely visible.

CASE VII.—Male, aged forty years. In his boyhood the patient had a boil on each cheek, which on healing left scars. That on the left cheek is now small, depressed, and white. That on the right began to change in 1889, forming a thin scale which gradually increased, then fell, and formed again. The lesion was scraped in 1891, and later was several times burned with acids and with the cautery, but it always recurred and spread. In October, 1902, there was a scar on the right cheek, bounded by a line extending from just below the inner canthus to the sulcus nasi, thence outward about an inch, upward to a spot about one-half an inch below and external to the outer canthus, and thence inward about a quarter of an inch below the free border of the lower lid to the point of origin. The border was elevated and dotted with firm, pearly nodules, which were most prominent along the upper border; similar nodules occurred in the scar itself. At the sulcus nasi was a depression about one-eighth of an inch deep, with hard borders. He received thirty exposures, aggregating three hours and fourteen minutes, between October 16, 1902, and January 2, 1903, when he stopped treatment on account of business affairs. There was a moist dermatitis over the lower part of the scar in November, but no more than a slight redness at any other time. At the time of the last treatment there was scarcely a trace of the disease—only

a little elevation along the outer and upper borders. In March, the area was entirely healed, and no nodules were visible, but in August, 1903, a nodule appeared in the right sulcus nasi. This twice broke down and healed again, hardly changing its size, and in September, 1904, the patient writes, it was still a small, firm, white nodule. The rest of the scar was normal.

CASE VIII.—Female, aged eighty-one years. In the summer of 1902 a small spot like a black-head appeared in the left labio-nasal fold. It grew very slowly for about six months, and then formed a scab, which fell, to be replaced by another, and this process continued, with gradual increase in the size and hardness of the lesion. On September 10, 1903, there was a thin, hard mass about one-half an inch across in the skin of the upper lip close to the left ala nasi. It was depressed in the centre, where the epithelium was wanting, and surrounded by a narrow red zone. Between September 10 and October 19 the spot received eleven exposures, aggregating fifty-nine minutes. The reaction never went beyond a slight redness. On October 29 the lesion was replaced by a pale, slightly depressed scar, which steadily became less conspicuous. At her last visit, June 1, 1904, the scar showed no sign of recurrence, and she wrote September 3, 1904, that it was still perfectly well.

CASE IX.—Female, aged seventy-five years. The patient first noticed a greasy, warty growth on the left side of the nose early in 1902. It grew worse in spite of local treatment, and by September 1, 1903, it was distinctly epitheliomatous. Between September 1 and September 16 the spot was exposed to the *x*-ray seven times, aggregating twenty-nine minutes. The patient then left the city. The lesion showed no change in that time, save an increase in redness, but it healed entirely during October, and the patient wrote, September 10, 1904, that it was still well, while a smaller patch on the nose, which she had declined to submit to *x*-ray treatment, remained, and was slightly inflamed at times.

CASE X.—Female, aged sixty-four years. In 1895 a small tumor appeared on the right side of the upper lip, about a quarter of an inch above the vermilion border. Between December, 1898, and January, 1902, it was scraped six times, and was treated with various ointments, but it always recurred, the last time in June, 1902. The growth was very slow, however, and in June, 1903, there was only a single pearly nodule, barely one-eighth of an inch in diameter, on the border of the small scar left by the previous curettings. Between June 20 and July 15 it received eight *x*-ray treatments, aggregating thirty-five minutes, and producing a mild dermatitis, which subsided quickly, leaving the skin perfectly smooth. The patient wrote September 5, 1904, that there was still no recurrence.

CASE XI.—Male, aged forty-one years. The disease began in January, 1901, as a cold sore. This was irritated by biting, and increased in size in spite of various local applications. On July 1,

1903, there was a hard, thick, slightly elevated mass about five-eighths of an inch in diameter, slightly eroded in places, and situated just to the left of the middle of the lower lip. It was exposed to the *x*-ray about every second day for two weeks in July, and again for two weeks in August, with slight improvement. The treatment was given also for five consecutive days in October, and for the four days ending December 25, 1903. The last two courses were much more severe than the first two, and were each followed by a considerable inflammatory reaction. This soon subsided, however, leaving the lip apparently normal. On August 17, 1904, the lip showed no induration whatever, only a faint scar, a little light in color at the border, but without nodules.

CASE XII.—Male, aged sixty-five years. The patient was a heavy smoker for many years, using a clay pipe. In the summer of 1902 he noticed a scab on the middle of the lower lip, and picked it off, but it formed again. After that the scab always returned after removal and the diseased area gradually increased in size, until in October, 1902, it formed a circular ulcer about three-eighths of an inch in diameter, with a pale, moist base, and firm, elevated and slightly everted border. The mass was tender only on the skin edge. It was exposed to the *x*-ray nearly every day from October 9 to November 8, with very little change. Between November 8 and November 19 the original tumor and an enlarged lymph node under the chin were removed at the City Hospital. A second operation was performed about June 21, 1903, for a recurrence in the glands under the chin, and the patient died three days later—of pneumonia, I was told.

CASE XIII.—Female, aged fifty-five years. About 1889 a wart-like spot appeared on the left side of the patient's nose. She picked it and it gradually developed a scab. About a year later it disappeared under mild applications, but recurred, and from that time on it was repeatedly scraped and cauterized, always recurring, and healing in one place only to advance in another. In October, 1902, the middle of the dorsum and left side of the nose were covered with a thin scar, while on the left cheek, about half an inch below the inner canthus, was a hard lump in the deeper layers of the skin, about a quarter of an inch in diameter, in whose lower quadrant was a shallow ulcer, extending also into the sound skin below. *x*-ray treatment was begun October 8, 1902, and was pursued faithfully. The ulcer soon healed, but the mass above it, while it diminished at first, did not disappear, although the exposures were pushed repeatedly to the production of a dusky redness, and even of a little exudation. The improvement was so slight that operation was advised, and the nodule was removed under ether September 22, 1903. The operation wound broke down in about a week, leaving a small, rather deep ulcer with infiltrated borders. *x*-ray treatment was resumed at once, and the ulcer healed quickly. As

before, the hardness was more resistant, but by August, 1904, it had nearly disappeared. The repeated exposures, however, had made the skin very tough and palpation was difficult.

CASE XIV.—Male, aged seventy-nine years. About 1901 a scab appeared in front of the right ear. This gradually spread and the skin beneath became indurated, and finally ulcerated. At first the growth was very slow, but for the last two or three months it was much more rapid. During this time the ulcer was treated with silver nitrate in solution, with mercurial ointments, and with hydrogen peroxide, which inflamed it greatly. April 4, 1904, there was an ulcer about one-quarter of an inch broad and three-quarters of an inch long, and surrounded by a red border one-eighth of an inch wide, immediately in front of the right ear. A little pus and serum exuded from the lower part of the ulcer. The tissue beneath was very firm and tense, and it was impossible to tell how much of the infiltration was inflammatory and how much was new-growth. Between April 4 and May 16 it received fourteen *x*-ray exposures, aggregating forty-six minutes. The ulcer had healed over by this time, and the mass was less hard, though considerable induration still remained. The patient then went abroad. He called again September 15, 1904, and reported that within two or three weeks of the last visit the skin seemed well and that he had no abnormal sensation. At present there is a single small pearly nodule at the site of the old lesion. But deep in the skin and in the subcutaneous tissue the old hard mass still remains, almost unchanged since May. *x*-ray treatment has been resumed and will be continued vigorously.

CASE XV.—Male, aged seventy-one years. Early in 1902 a small papule, covered with a crust, formed on the patient's left cheek near the nose. It spread gradually, and late in the year, after *x*-ray treatment by another physician, became inflamed. When first seen in January, 1903, it formed a protuberant mass about three-quarters of an inch long and half an inch broad, very red, and moist in places. Under mild ointments the inflammation subsided, leaving only a slight induration. A single *x*-ray treatment was given in April. The patient did not return until September, when the induration had spread and the skin had ulcerated. Again the ulcer healed under the *x*-ray, and the induration diminished, and again the patient disappeared for five months, returning in April, 1904, with a hard mass three-quarters of an inch long by one inch wide, situated in and beneath the skin about three-quarters of an inch below the left eye. The upper part was about a quarter of an inch thick—the lower part thinner, and the whole slightly movable on the bone. The *x*-ray treatment was resumed and the reaction carried twice to a marked dermatitis, resulting in a diminution in the size of the growth, when again the patient disappeared. He returned in September, 1904, the tumor having increased in size and hardness, and having again ulcerated in the middle.

CASE XVI.—Male, aged sixty-six years. The patient noticed for eight or ten years a wart-like growth on the right ala of the nose. It varied in size, but was never larger than a split pea. Two or three months before applying for treatment he noticed a scab forming on this wart; it fell from time to time, but always was renewed, and during the last six weeks there was a persistent and growing ulcer. When first seen, in April, 1903, there was an irregular ulcer about one-eighth by three-eighths of an inch, on the right ala of the nose, with an indurated border, and a pale, uneven base exuding a slight serous discharge. The induration extended beyond the border. Between April 8 and May 6, 1903, the ulcer received eight treatments, aggregating forty minutes. In this time the ulcer healed but an indurated pearly area remained, and a month later there was a patch of firm epitheliomatous tissue about one-sixteenth of an inch broad by one-half an inch long, with two narrow cracks covered with brownish scales. But the patient considered himself cured, and stopped treatment. I have not seen him since, but he writes, September 10, 1904, that there was little change until last winter, when the disease grew worse, and again improved under *x*-ray treatment. This summer, for the third time, the growth increased its activity, and is now under *x*-ray treatment.

CASE XVII.—Female, aged forty-one years. The growth appeared in November, 1902, as a yellowish papule with a black centre, on the right side of the nose. It was irritated by pricking, and gradually increased in size. It was curetted January 12, 1903, but very incompletely, and then it grew more rapidly than ever, forming, on January 22, an ulcer a quarter of an inch broad and half an inch long, with a hard, raised edge, sloping sides, and a dry, yellowish base, surrounded by a narrow zone of inflammation. Between January 22 and March 2 it received twelve *x*-ray treatments, aggregating one hour and sixteen minutes. The ulcer had diminished one-half, and the edge had grown much softer. The patient called but once again, April 16, 1903, when an exposure of ten minutes was given, and she has not been heard from since.

CASE XVIII.—Male, aged eighty-six years. A little over two years before applying for treatment the patient noticed on the left temple a little indentation covered with a crust, and ascribed it to a razor cut. The crust alternately formed and fell, the lesion steadily growing until January 17, 1903, when it was half an inch in diameter, with a raised, pearly, indurated border and a red, scaly, slightly depressed base, which bled easily. It responded readily to *x*-ray treatment, and had nearly disappeared, when on March 30, 1903, the patient died from the rupture of an artery, after an illness of eight hours.

No.	Age	Site.	Duration before treatment.	Period of treatment.	Result.
1	41	Temple.	12 years	2½ mos.	No recurrence after 1 year and 5 months.
2	78	Front of ear	2 "	1 yr. 7 mo.	" " " 4 months.
3	59	Lower eyelid	7 months	5 months	" " " 8 "
4	76	Cheek	6 "	1 day	" " " 5⅓ "
5	61	"	7 "	6 weeks	" " " 1 year and 9 months.
6	76	"	2-3 years	1 month	" " " 10⅓ months.
7	40	"	18 "	2½ mos.	Recurred after 7 months.
8	81	Nasolabial fold	1 year	5½ weeks	No recurrence after 10⅓ months.
9	75	Nose	1½ years	2 "	" " " 1 year.
10	64	Skin of upper lip	8 years	4 "	" " " 1 year and 2 months.
11	41	Lower lip	2½ years	6 months	" " " 8 months.
12	65	" "	2 months	1 month	No improvement; operation. Death after operation for recurrence 6 mos. later.
13	55	Cheek	18 years	1 yr. 10 mo.	Improved; growth never entirely removed.
14	79	Front of ear	3 "	6 weeks	Improved; ceased treatment.
15	71	Cheek	1 year	1 yr. 3 mo.	" irregular treatment.
16	66	Nose	3 months	1 month	" ceased treatment.
17	41	"	2 "	5½ weeks	" " "
18	86	Temple.	2 years	2½ mos.	" death from intercurrent disease.

Of the whole series of 18 cases, 1 (Case XVIII.) died of intercurrent disease and 4 (Cases XIV. to XVII.) were too brief or too irregular in their attendance to get permanent results. Of the remaining 13 cases, in whom the method had a fair trial, 1 case (Case XII.) showed no improvement after one month of treatment; in 1 (Case XIII.) the condition was improved, but the growth never entirely removed; and 1 (Case VII.) was apparently cured, but had a recurrence seven months later. The remaining 10 (77 per cent.) showed no recurrence after periods ranging from four months to one year and nine months.

Case XII., who showed no improvement, had a rapidly growing epithelioma of the lower lip—a type now recognized as being very difficult to heal with the *x*-ray. Still, it is possible that longer and more vigorous exposures might have arrested the growth, as indeed happened in Case XI., and it is very probably that his death was due directly to an inhalation pneumonia dependent on the second operation.

Case XIII., in whom the growth never entirely disappeared, was very similar to cases XIV. and XV., who also were very hard to influence. The distinguishing mark in all three was an almost stony hardness deep in the skin and the subcutaneous tissue, covered in great part or entirely with apparently normal epithelium, and showing very little tendency to ulcerate. The ulcer, if present, heals readily, but the hard mass beneath yields slowly or not at all. They require very intense treatment, and I believe that many of this class cannot be cured by the *x*-ray unless an ulcer is produced.

In marked contrast with this type of epithelioma is that represented by Cases I. to X. and Cases XVI. to XVIII. The common and characteristic mark of this group is the superficiality of the lesion. The induration seems to be in the skin itself, and quite

near the surface—never deep, as in the resistant type. The borders are generally narrow, slightly elevated, firm, grayish-white, and composed either of separate pearly nodules or of such nodules run together to form a ring or part of a ring. The base is sometimes fairly deeply excavated, as in Case V., but usually it is only a little below the level of the surrounding skin. It is sometimes bright red, and moist from exuded serum, but the exudation is never very great, and often dries to a scab, which falls from time to time, or which may be pulled off, leaving a moist, easily bleeding surface; or the base may be only delicate pink scar tissue. In the above series but one case of this type (Case VII.) recurred.

Before closing there is another class to be mentioned, for whom *x*-ray treatment is invaluable—a class dependent on the patient rather than on the type of disease. It includes that large group of cases in which any radical operation is impossible, is inadvisable, or is refused. Besides the frankly inoperable cases which every surgeon knows, and those whose horror of the knife is such that any cutting operation is out of the question, there are many patients who by reason of age or of bodily infirmity would be placed in much greater danger by an operation than they suffer from their disease. Case II. is a good example. He is a man of seventy-eight years, in good general health, but not strong enough to run the risk of a general anæsthetic. He is now, four months after his last treatment, absolutely free from all signs of recurrence. But even should the growth return there is every reason to believe, from his previous history, that it could at least be held in check, and long before he could suffer any inconvenience from it he will probably die from some intercurrent disease—as actually happened in Case XVIII. For such cases the safety, the convenience, and the painlessness of the method are its great advantages; and to these advantages we may add, if the lesions be superficial, a reasonable hope of permanent cure.

A STUDY OF ACUTE HEMORRHAGIC ENCEPHALITIS (STAPHYLOCOCCUS PYOGENES AUREUS).

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Following is a study of encephalitis in man, due to the staphylococcus pyogenes aureus. Parallel lesions have been studied in

guinea-pigs, with a view to establishing the time limits and order of the acute inflammatory changes.

A text for the present work was afforded by some points of a case, previously reported at length,[1] of cortical hemorrhages ensuing upon subinfection with the staphylococcus pyogenes aureus during convalescence from scarlet fever in a boy aged five years. An abstract of this case follows:

CASE I.—*Abstract.* About five weeks after onset of scarlet fever, convalescence was interrupted by cerebral symptoms, and death occurred two weeks later (seven weeks after admission). The contractions and sensory symptoms began in the right leg and advanced during four days to affect the whole right side, including the face. The contractions were sharply defined (at one time alternating regularly with relaxations at intervals of about ten seconds) and limited in duration (a few minutes). Paralysis of the affected limbs ensued. During the last week the child was in the main unconscious (masking symptoms on left side).

At autopsy the organs and tissues showed little gross evidence of lesion, beyond desquamation of skin and fresh and pigmented hemorrhagic lesions in the cortex of both parietal lobes, with œdema of overlying pia mater.

Microscopic study showed an early bronchopneumonia and septicæmia (staphylococcus pyogenes aureus) and a purulent inflammation of foci in the parietal pia mater and overlying arachnoidal villi. Besides large areas of hemorrhage in the cortex, there was extensive development of cells phagocytic for polynuclear leukocytes, blood corpuscles, and fatty detritus. These phagocytes lay in meshes of the pia mater and in the adventitia of the short arteries of the cortical system. The phagocytosis was accompanied by solution and fatty changes of adjacent nerve tissues. Fatty changes in associated motor systems and early changes (axonal degeneration of anterior horn cells by Nissl method) in the lower motor systems.

The interpretation of Case I. is not wholly clear. Suspicion, however, attaches to the staphylococcus pyogenes aureus and its toxins for the production of some of the cerebral lesions. A study has therefore been made of further accessible cases of septicæmia and encephalitis associated with the staphylococcus aureus to find what aspects are held in common. Abstracts of these cases follow:

CASE II.—*Clinical History.* A. B., a girl aged twelve years, was admitted to Dr. G. C. Sears' service at the Boston City Hospital January 7, 1901. On entrance she was wildly delirious. Her head was retracted, and there was spasm of the posterior cervical muscles, with inability to flex the head. The pupils were widely dilated and failed to react to light. Both tonsils were enlarged, and the tongue

[1] E. E. Southard and F. R. Sims. A Case of Cortical Hemorrhages following Scarlet Fever, Journal of the American Medical Association, September 17, 1904.

bore a heavy white fur. There was a loud, rough, systolic murmur audible throughout the heart area, but at its maximum in the second left intercostal space and over the apex. The murmur was transmitted into the vessels of the neck, the axilla, and the back. There were a few moist rales at bases of lungs behind. The abdomen was everywhere tympanitic, and there was slight voluntary spasm of the walls. The reflexes were normal. Over outer aspect of right ankle, extending from a point 18 cm. above external malleolus to the heel, was an erythematous swelling, acutely tender and painful on passive motion. Below malleolus were three small pustules with incised (surgical) wound.

The origin of this condition is unknown. Four days before she had the first symptoms of her illness, chilly feelings and frontal headache. The next day small black spots were noted on the right foot, and an incision was made. The next day (third of the attack) she vomited after meals. Then gradually supervened the condition at entrance as above described.

The girl was fairly well developed, but poorly nourished. She is said to have had rheumatic fever at six years of age, scarlet fever at nine, measles at ten, and was just recovered (five weeks) from diphtheria. It is not possible to say what importance attaches to any of these events.

The day after entrance fresh inflammatory areas developed over the head of the fifth metatarsal bone of the left foot and the inner aspect of the left wrist. The leukocytes were but 10,000 per c.mm. The patient immediately vomited the food administered by nasal catheter.

The evening of the third day after entrance the patient died without notable change of condition.

Clinical Summary. Girl, aged twelve years, just recovered from diphtheria, with history of rheumatic fever, scarlet fever, and measles. Onset of attack, chilly feelings, and frontal headache, with development of purulent hemorrhagic areas on right foot, and vomiting two days later. Four days after onset, admitted in delirium, with suppurating wound of heel and heart murmur. Retraction of head. Dilatation of pupils, which failed to react to light. Development of fresh superficial inflammatory areas. Death eight days after onset of symptoms.

The autopsy was performed by one of us (E. E. S.) January 10, 1901. Following are the findings in the head:

Brain, weight 1200 gms. Dura tense, convolutions somewhat flattened. Density of brain about normal except right occipital lobe, which is semifluctuant. On section there is found near the apex of this lobe a rather firm, irregular mass of clotted blood, 3 cm. in greatest diameter. It reaches to within 1 cm. of surfaces of brain, but does not show externally. Around the clot is more or less fluid blood. The adjoining brain tissue for some distance is

stained reddish-brown and is of soft consistence. The hemorrhage has extended into the right lateral ventricle, where fluid blood is present. A little is present also in the left ventricle.

Anatomical Summary. Wound of heel, with purulent infiltration of adjoining tissues; infective thrombus left ventricle wall; multiple abscesses of heart wall, kidney, adrenal, liver, spleen, intestines; diffuse small hemorrhages of lungs, kidney, epicardium; hemorrhages and softening of right occipital lobe; fatty degeneration of myocardium and skeletal muscles; chronic endocarditis (mitral); chronic adhesive pericarditis; chronic pleuritis of left lung and right apex.

Microscopic Findings. Cultures from the organs showed a septicæmia due to the staphylococcus pyogenes aureus. The growths were pure except from the kidney, which showed, besides the staphylococcus, an organism of the colon-typhoid group.

The histological examination of the various organs confirmed the diagnoses from gross findings. The lung shows small hemorrhages, chiefly without leukocyte reaction. The marrow of the femur is very cellular, containing numerous leukocytes of the mononuclear series, but very rare polynuclear leukocytes.

Special study of tissues from the brain was made by a variety of methods.

The subcortical lesion in the occipital lobe shows wide sheets of clear, well-preserved blood, with occasional polynuclear leukocytes and several foci of staphylococci, both free and within cells. The hemorrhage penetrates the cortical tissue along lines of least resistance between the radiating bundles of nerve fibres. Occasionally large vessels from the cortical system run free through the blood, with the adventitial meshes dilated with polynuclear leukocytes and occasionally embraced by areas of coarse fibrin. Near the vessels there occur purulent areas, with fatty changes, pigment, fat-containing and pigment-containing phagocytes, and without notable evidence of repair. Adjacent to the hemorrhagic areas the myelin, as a rule, stains perfectly; but a few fibres are represented in Marchi sections by linear collections of black dots. The nerve cells occasionally show changes, as a rule attributable to swelling or shrinkage due to œdema. These changes are scarcely more marked near the hemorrhage than remote from it.

Case III.—*Clinical History.* H. H., a man, aged twenty-two years, was admitted to Dr. G. B. Shattuck's service at the Boston City Hospital, December 5, 1903. On entrance he was unconscious and restless, with flushed cheeks and equal, contracted pupils, reacting sluggishly to light. There was slight rigidity and retraction of neck. The abdomen was slightly retracted and rigid, with tenderness over pubes. The legs were flexed and rigid. The hands and feet were blue, and there were irregular hemorrhagic areas about thumbs and over outer surfaces of both feet and the toes.

The knee-jerks were normal. Kernig's sign and Babinski's sign were absent.

The attack had begun the day before, with increase in frequency of micturition and general discomfort. The physician, Dr. C. L. Knight, had forthwith suspected cystitis, as he had had the patient under treatment for some time for urethritis. In the afternoon of the day before admission the patient complained of severe pains in various parts of the body, especially the thumb and ankle. Nausea, vomiting, and delirium followed.

The day after admission (the third day of the symptoms) the patient died, without marked change of condition. The pulse, at first of moderate rate, later became rapid, small, and easily compressible. Cyanosis increased. The chest became filled with moist rales. The ecchymoses of the extremities slowly increased in extent. The pupils became widely dilated and still reacted sluggishly to light. The reflexes remained as before; there was some question whether Babinski's sign was present.

Clinical Summary. Man, aged twenty-two years, with history of treatment for urethritis. Onset of attack with increased frequency in micturition and malaise. Later in the day various focal pains, nausea, vomiting, delirium; cyanosis; ecchymoses on thumb, ankles, and toes. Pupils at first contracted, before death dilated. Death on the third day.

Autopsy Findings. The autopsy was performed by Dr. R. L. Thompson and one of us (E. E. S.) December 7, 1903. The findings in the head were:

Head. Hair dark and fairly thick. Scalp normal. Cranium of the usual thickness. Dura externally smooth and tense. Sinuses contain fluid blood with cruor clot. Pia over left hemisphere almost dry, and tightly stretched over flattened convolutions and effaced sulci. There are a number of irregularly distributed ecchymoses, varying in diameter from a pin's head to 0.5 cm. or more, rarely 0.75 cm., either within meshes of pia at lips of sulci or shining through from cortical substance. In the region of the left supra-angular gyrus are two well-defined ecchymoses, with irregular and re-entrant borders (0.5 cm. and 0.75 cm. in diameter, respectively), containing in the middle pinhead foci of frank, yellowish-green pus. The pus has not broken through the pia. Pia over right hemisphere contains a slight amount of clear fluid, but is externally almost dry. Effacement of sulci by pressure has just begun. Pia on both sides shows a well-marked injection, with minute, tree-like tracery in the superficial cerebral venules. About some ecchymoses are delicate pink areas of diffused blood pigment (some of which may be of post-mortem origin). Vessels at base normal.

Cerebrum. The core of the left occipital lobe is replaced with a walnut-sized mass of loosely clotted blood, resting in a bed of moist, grumous, pinkish-gray detritus. Beyond the zone of dis-

integration is œdematous white matter, with distinct puncta cruenta and minute hemorrhages. The cortex of the occipital pole is destroyed, and the hemorrhage points also upon the posterior horn of the left lateral ventricle, into which has oozed several cubic centimetres of blood, now clotted *in situ*, with a little staining of posterior portion of choroid plexus. There is no gross evidence of old abscess or other lesion than hemorrhage in this area. It is probable that the hemorrhage is from a medullary branch or branches of the cortical arterial system.

The core of the right occipital pole shows a similar area of hemorrhage (from the medullary branch of the cortical arterial system), thimble-shaped, giving destruction chiefly of white substance with a small portion of cortex. The pia is just tangent to the lesion, which is, therefore, scarcely evident from without.

The substance elsewhere is slightly moister than usual, and both cortex and white matter contain fairly numerous, pinhead, purplish areas of hemorrhage, without evidence of pus. These areas are somewhat more frequent on left side. The substance on section shows a slight retraction of white matter (or release of tension in gray?) and a diffuse appearance somewhat suggestive of encephalitis, but there is no relatively normal white substance with which to compare.

The basal ganglia and lower system are spared from lesion. There are a few ecchymoses in the cerebellum.

Brain. Weight 1265 gms.

Anatomical Summary. Acute endocarditis; acute pericarditis; multiple abscesses of liver, kidney, and thyroid; infarcts of small intestine; acute splenitis; hyperplasia of mesenteric lymph nodes; acute fibrinous pleuritis (left); œdema and congestion of lungs; acute purulent bronchitis; interstitial orchitis; œdema and congestion of brain; multiple ecchymoses of white and gray matter; abscesses of cortex; hemorrhages into occipital poles (probably from medullary branches of cortical arterial system).

Microscopic Findings. Cultures from heart's blood, pericardium, mitral valve, liver, spleen, kidney, right centrum semiovale, left occipital lobe, and abscess on heel showed staphylococcus pyogenes aureus.

Histological examination of the organs of the trunk showed in the main the lesions diagnosed from gross appearances. The kidney shows a focal chronic interstitial process.

In the subcortical regions of certain foci in the cerebrum and the cerebellum are well-defined abscesses of a characteristic type. A central colony of staphylococci is surrounded by polynuclear leukocytes in a zone, which is in turn surrounded by a zone of fresh hemorrhage. These areas are sometimes a millimetre in diameter, but are, as a rule, merely punctiform. Beyond the lesions there is usually no sign of tissue reaction.

CASE IV.—*Clinical History.* M. M., a woman aged forty-two years, was admitted to Dr. G. C. Sears' service at the Boston City Hospital March 14, 1902. On entrance she was mildly delirious. There was well-marked sclerosis of all palpable arteries, and the heart showed at the apex short systolic and presystolic murmurs, heard also in axilla and back; a systolic murmur was audible at base and in aortic and pulmonary areas. The right lung was dull below the fifth rib in the axillary line (respiration and vocal resonance distant, tactile fremitus diminished). There were friction sounds opposite the right fifth rib. The left base showed many moist rales. Abdomen, dull in flanks, showed fluid wave. There was considerable œdema of ankles and legs. The pupils were equal and reacted normally.

The woman is said to have had influenza three years before, after which she had suffered from dyspnœa, palpitation, and frequent micturition. The menopause had occurred three months before onset of present illness. For four months she had had a slight cough. A week before entrance she had taken to bed with a sharp attack of pain in the right chest, followed by rapid and progressive increase in dyspnœa and increase of cough, with frothy expectoration.

After admission her condition grew worse; she became noisy and garrulous and required restraint. A week after admission she got out of bed during the night and injured her right eye. The upper lid had to be incised some days later, and two drachms of pus were evacuated. Constipation set in, with palpable fecal masses over abdomen. The orbital suppuration grew gradually better, but on the twenty-third day after admission (two weeks after injury to eye) an erysipelas-like condition developed about the eye. Thenceforward the patient gradually failed, and a week later died.

Clinical Summary. Woman, aged forty-two years, just after menopause, with arterial and cardiac sclerosis. Pleurisy with effusion, gradually deepening delirium, injury to eye with suppuration (a week after admission, two weeks after onset of pleurisy), and constipation. Death three weeks after injury to eye, a week after development of erysipelas-like condition about eye, two days less than a month after admission.

Autopsy Findings. The autopsy was performed by Dr. W. R. Brinckerhoff April 14, 1902. The findings in the head were:

Brain. Weight, 1270 gms. Dura and sinuses normal.

Middle Ears. Normal.

On the external aspect of the right temporal lobe is a small abscess (3 mm.) surrounded by a zone of injection. Similar smaller abscesses are present over the vertex. On section, ventricles contain considerable amount of clear, straw-colored fluid. The substance of the cerebrum appears normal. Cerebellum normal. In the middle of pons is a circular area 6 mm. in diameter, which is some-

what soft and of a black color. This area is sharply circumscribed. Its greatest diameter is lateral, not appearing in the adjacent sections 5 mm. apart. The surrounding brain substance appears normal.

Anatomical Summary. Pleurisy with effusion (right side); hydropericardium; multiple abscesses of heart, kidneys, spleen, lung, and brain; ulcerative colitis and proctitis; chronic diffuse nephritis; acute cystitis; uterine fibromyoma; general arteriosclerosis; chronic splenitis; small hemorrhage in pons.

Microscopic Findings. Cultures from liver, spleen, and kidney showed pure growths of staphylococcus pyogenes aureus. Histological examination of the various organs confirmed the diagnosis of septicæmia. No cultures were taken from the brain abscesses, which were saved entire for histological purposes; but there can be no doubt of the relation of the staphylococcus to the abscesses. The special points in the histology of this case are brought out in the following:

The lesions beneath the pia mater of the temporal lobe, for example, consist of a central colony of staphylococci in and about a vessel which is surrounded by a zone of polynuclear leukocytes, often phagocytic for the bacteria. Among the polynuclear leukocytes are numerous larger phagocytes, now of the compound granule type, elsewhere containing chromatic material derived, as a rule, from polynuclear leukocytes. The large phagocytes sometimes contain bacteria as well as remains of tissue cells. Outside the zone of polynuclear leukocytes is a broader zone, consisting almost purely of cells of the phagocyte group, here in most instances of the compound granule type. Beyond these zones of nucleated cells is a zone of pure and well-preserved blood. There is nowhere any notable amount of fibrin. There are in many places small vessels plugged with staphylococci, some of which have grown post-mortem.

The sections from the pontine lesion are of note by reason of the juxtaposition of the fresh hemorrhagic lesions with an older cystic lesion. The older lesion consists of a small cavity, about 2 mm. in diameter, lined by a condensed layer of neuroglia and filled with large, vacuolated phagocytes and granular material. The neuroglia lining is interrupted in places by slender projections due to vessels invested by a thin layer of oval, fibrillated glia cells. The fresh lesions show blood free in the meshes of the tissue, with here and there a large phagocyte and polynuclear leukocyte and without notable amounts of fibrin. The surrounding tissue shows no reaction beyond an increase in the volume of the cell bodies in some neuroglia cells.

Case V.—*Clinical History.* J. C., blacksmith, of middle age, was admitted to Dr. A. L. Mason's service at the Boston City Hospital December 3, 1897. He was brought to the hospital

delirious and unconscious in an ambulance, having fallen in the street.

Physical examination showed the left pupil slightly larger than the right, knee-jerks absent, pulse feeble but regular, chest slightly hyperresonant, pleural rubs in left axilla and lower back, and a temperature of 104°. The urine showed 0.5 per cent. albumin. The patient died the day after admission without change of condition.

Autopsy Findings. The autopsy was performed by Dr. F. B. Mallory December 4, 1897. The findings in the head were:

Brain. On the right side of the pia 3 cm. from the median fissure, and in the sulcus just back of the fissure of Rolando, were three, minute, yellowish specks, apparently miliary abscesses. The surrounding brain tissue was œdematous and swollen and the pia contained minute hemorrhages. In the substance of the brain no lesions could be found anywhere.

Middle ears normal.

Sinuses of nose and the antrum of Highmore on each side were all normal.

Anatomical Summary. Septic infarctions of lungs; metastatic abscesses of kidneys and meninges; acute fibrinous pleurisy; chronic adhesive pleurisy; congestion of lungs.

Microscopic Findings. Cultures from organs of the trunk showed pure growths of the staphylococcus pyogenes aureus, except that from the kidney, which showed also an organism of the colon-typhoid group.

Histological examination confirmed the diagnosis made from gross appearances. The liver shows some cellular infiltration of the portal spaces and central congestion.

The histological picture presented by the brain varies from a simple meningitis to a diffuse meningoencephalitis. The simple meningeal inflammation consists of an exudate of polynuclear leukocytes, more thickly into the proximal meshes of the pia mater. There is strikingly little blood and a small amount of fibrin in this lesion. There are fewer meningeal phagocytes than usual; but a few lymphatic clefts are filled with such cells containing fragmented polynuclear leukocytes. The exudate follows the cortical arteries into the brain substance in some cases as far as the white matter. The subpial neuroglia and the pyramidal cell layers are for long distances dotted with polynuclear leukocytes of fairly even distribution. It is unusual to find polynuclear leukocytes in apposition with nerve cells. The nerve cells are slightly swollen. The bodies of the neuroglia cells are, as a rule, invisible; but some of the cells of the subpial layer approach the astrocyte in type.

CASE VI.—*Clinical History.* A. M., an Irish woman aged thirty-three years, was admitted to Dr. J. N. Coolidge's service at the Boston City Hospital June 15, 1904. On entrance she was

delirious, half-conscious, and unable to answer questions. There was convergent strabismus and a choreiform or athetoid tendency to co-ordinate movements of both arms. Nothing further was discovered in the physical examination to throw light on the condition. The present illness was said to have lasted ten days, setting in with vomiting, which continued for five days. The strabismus was developing meanwhile, and the twitchings became well marked. She was sleepless and complained of soreness in the abdomen. For years she had been addicted to the use of alcohol, often to excess. The patient died five days after entrance. The choreiform movements persisted until death. The convergent strabismus became more marked. Stiffness of neck developed. The reflexes remained normal.

Clinical Summary. Woman, aged thirty-three years, with history of abuse of alcohol, died in delirium fifteen days after onset of an attack of choreiform character, with convergent strabismus, insomnia, and normal reflexes. Onset with vomiting, lasting five days.

Autopsy Findings. The autopsy was performed by Dr. S. B. Wolbach June 21, 1904. The description of the head by one of us (E. F. S.) follows:

Head. Scalp normal; skull symmetrical; frontal suture effaced. Superciliary ridges and frontal eminences ill-defined. Calvarium opaque by transmitted light and everywhere moderately thickened. The thickening affects chiefly the inner table, and is least marked at the bregma, where the internal surface presents a shallow, diamond-shaped depression corresponding to the anterior fontanelle. The frontal bone shows marked symmetrical thickening, which transforms inner arc to an oblique flat surface, on which there is a slight groove for the superior longitudinal sinus and a few narrow depressions for the meningeal vessels. At a point 4 cm. from the orbit the bone is 1.5 to 2 cm. thick. The diploë is nowhere well marked. The frontal bone is ivory-like on section and of the consistence of the petrous bone. Dura normal. The dura beneath frontal bone is readily separable from the inner table. Sinuses and meningeal veins contain fluid blood. Pial vessels everywhere injected. Arachnoidal villi well developed. Pia of vertex œdematous. Substance moist. Everywhere elastic except in an ill-defined area, including second right temporal convolution. The cortex and underlying white of this region are plastic and readily crushed; the puncta cruenta of the white matter are distinct, and there are a few minute, perivascular hemorrhages. Co-ordinate areas in the left hemisphere are equally moist; but the gray matter does not bulge from the plane of section. The rest of the centrum semiovale shows no more than œdema.

The frontal convolutions are fairly symmetrical. There is no microgyria and no narrowing of gray matter, but there is a slight

increase of consistence in the frontal gyri on comparison with, for instance, the occipital gyri. The frontal and especially the prefrontal region as a whole may be looked on as undersized. Rest of encephalon and spinal cord show less œdema than the hemisphere and no further gross lesion.

Middle ears normal.

Anatomical Summary. Œdema and congestion of lungs; chronic fibrous pleuritis (left); œdema of pia; cerebral œdema; focal softening of right second temporal convolution (encephalitis); frontal lobes undeveloped; thickening of cranium (most marked in frontal bone).

Microscopic Findings. Cultures from organs of the trunk remained sterile. Culture from the white matter beneath the second right temporal convolution showed staphylococcus pyogenes aureus, together with a few colonies of similar appearance which never assumed a golden-yellow color (staphylococcus pyogenes albus?). A culture of the staphylococcus pyogenes aureus derived from this case was used in a portion of the inoculations described below.

Examination of the organs of the trunk showed nothing adequate to account for the history of the case. The lung shows a few *Herzfehlerzellen* in some alveoli and a few bronchi plugged with polynuclear leukocytes in good preservation and without bacterial inclusions. The spleen shows an unusually high percentage of polynuclear leukocytes and fairly numerous eosinophilic leukocytes in the pulp, but is otherwise not remarkable. The liver is slightly fatty; some of the cells central in the lobules are lace-like. The kidney shows a few slender casts in the tubules of the pyramids. Otherwise both the organs mentioned and the others examined show little that is noteworthy.

Co-ordinate places in the hemispheres were examined to detect the extent and nature of the inflammatory process suggested by the gross appearances and the bacterial findings. The two sides are distinguished by the fact that, in the section taken from the cortex and white matter of the right temporal lobe, there are numerous small collections of blood globules, with a few polynuclear leukocytes lying in the meshes of the arterial adventitia. There seldom occur, however, hemorrhages of any great volume. Blood rarely occurs free in the tissue. On comparison with tissue from the opposite hemisphere it is found that very many more distended capillaries have become visible in the cortex and notably in the subcortical region of the right temporal lobe. Several of these capillaries are found packed with polynuclear leukocytes. The neuroglia shows no pertinent differences on the two sides; the subpial glia of the left hemisphere appears denser in structure than in the right in the places examined. Numerous nerve cells are contracted and somewhat densely staining by several of the technical methods employed (eosin and methylene blue, aniline blue con-

nective tissue, and phosphotungstic-hæmatein methods, for example). These cells are possibly more numerous in the left hemisphere than in the right in the places examined. These latter changes are certainly not beyond the range of artefact and are scarcely entitled to specific importance on account of the omnipresent œdema. Yet these cells recall the cells found in certain foci of our experimental material. The cerebellum and the rest of the nervous system as far as examined showed no noteworthy lesion. A few capillaries in the choroid plexus contain numerous polynuclear leukocytes; there is a much smaller number outside the capillaries and none beyond the ependyma.

General Clinical Summary. From the histories detailed above the following *résumé* has been drawn:

Three of the patients were male, three female. Their ages varied from five to fifty-five years.

In every case, excepting Case V., whose past is unknown, there is a history of antecedent disease; thus Case I. was convalescing from scarlet fever; Case II. was five weeks recovered from diphtheria and had a chronic endocarditis of long standing; Case III. was under treatment for chronic urethritis; Case IV. had pleurisy with effusion and was but three months beyond the menopause, and Case VI. had a history of excess in alcohol of many years' duration.

The onset was in three cases sudden (hemiparesis and unilateral convulsions in Case I.; chilly feelings and frontal headache followed by ecchymoses in Case II.; malaise, manifold pains, ecchymoses, and cerebral symptoms in Case III.). Case V., in which the onset is unknown, was in all ways fulminant. In Case IV. the symptoms gradually supervened upon the pleurisy and the orbital suppuration. Case VI. showed a gradual onset.

The syndromes as a whole were of pronouncedly cerebral type in Cases I. and VI., of meningitic trend in Cases II. and III., of septicæmic character in Case IV. Septicæmia could be suspected in all three cases (II., III., IV.) in which superficial ecchymoses or suppuration became prominent.

The temperature varied for the various cases: at times 103° and 104° for cases III. and V.; the temperature in cases II., IV., and VI. was never high and frequently subnormal.

The pulse was in no case subnormal, and, as a rule, ranged above 100. The respirations were, as a rule, increased.

The duration of the encephalitic symptoms cannot in all cases be closely reckoned: Case III., three days; Case IV., one week (after development of erysipelatoid condition) or three weeks (after injury to eye); Case II., eight days; Case I., two weeks; Case VI., fifteen days; Case V., unknown. Thus those cases were of longer duration in which the cerebral syndromes were most clearly marked.

General Anatomical Summary. Of the gross findings at autopsy the following are to our present purpose: chronic lesions

which might correspond with greater likelihood of bacterial infection were found in several cases; thus, the remains of scarlet fever in Case I., chronic endocarditis in Case II., arteriosclerosis in Case IV.

The phenomena of general infection were found in Cases II., III., IV., and V. Comment is made below upon the correlation of pulmonary lesions with our cases.

The distribution of the brain lesions is as follows:

Four cases (I., II., III., IV.) showed areas of frank and somewhat voluminous hemorrhage, as a rule involving primarily the subcortical region (of the vertex in Case I., of the occipital lobes in Cases II. and III.), and in Case IV. affecting the pons.

Three cases (III., IV., V.) showed multiple ecchymoses and small abscesses of the cortex or subcortical region, with or without gross evidence of surrounding œdema.

In three cases (I., V., VI.) œdema of pia mater was remarked.

In two cases (II. and III.) there was noted an effusion of blood into the lateral ventricles; and in these cases the convolutions were flattened.

In two cases (IV. and VI.) in which the temporal lobe was involved the middle ears showed no lesion. The mucosæ of the head play no such role in this kind of encephalitis as in the massive brain abscesses made familiar by Macewen.

General Summary of Microscopic Findings. The staphylococcus pyogenes aureus was found in all cases in culture post-mortem, generally distributed in five cases, in the brain alone in Case VI. The diagnosis of general infection, at least at the time of death, seems warranted in the first five cases. Case VI., in all ways unusual, may possibly be interpreted as showing the first stage of a massive brain abscess; but the middle ear showed no lesion at autopsy. The atria of infection remain obscure in Cases V. and VI. In Cases II., III., and IV. acute endocarditis was found; and, although in none of these cases is the chain of evidence entire, there were present in all three adequate primary lesions (suppurating surgical wound in Case II., chronic urethritis in Case III., colitis in Case IV.).

The microscopic findings in the organs at large call for little comment. Focal pulmonary lesions were either grossly prominent or made out microscopically in all six cases. There was pus in the bronchi of Cases III. and VI., bronchopneumonia in Case I., and there were septic areas of hemorrhage in the lungs of Case II., septic infarction in Case V., and multiple abscesses in Case IV. This coincidence of pulmonary and brain lesions is certainly of clinical importance. A similar coincidence was noted at least as early as the sixties of the last century.[1] Compare also the production described below of meningitis and meningoencephalitis in the

[1] Biermer, Zur Theorie und Anatomie der Bronchienerweiterung, Virchow's Archiv, 1860, xix. S. 244.

guinea-pig by intrapulmonary inoculations. We are not prepared at present to regard this coincidence as a matter of cause and effect.

The microscopic findings in the brains of this series of cases present more features in common than the gross findings. Thus, whereas miliary abscess, punctiform or massive hemorrhage, and ill-defined red softening form quite diverse gross pictures, the microscopic pictures form unitary series or are well-nigh interchangeable.

It is, moreover, by no means scholastic to insist that too close lines cannot be profitably drawn between meningitis and encephalitis. The word "extension" has gained so wide a vogue that one forms the idea that, although a process may extend, the diagnosis somehow should not extend *pari passu*. Meningitis by extension from abscess and encephalitis by extension of pial inflammation are processes of importance, though charged with being merely secondary. It is these secondary phenomena, in especial the encephalitic ones, which, in the cured cases, may afford a basis for our so mysterious scleroses.

The inflammation of meninges and cortical and subcortical substance in man produced by the staphylococcus pyogenes aureus is distinctively hemorrhagic. Very little fibrin is formed in these lesions. The bleeding continues in some cases until stopped by intracranial pressure. Small vessels are, as a rule, affected.

The typical picture is of a central colony of staphylococci in and near a vessel surrounded by zones of polynuclear leukocytes, large phagocytic cells, and blood. Dying nerve cells are sometimes included in the lesion. The neuroglia cells are slightly active about some of the lesions. Fibril production is absent. The myelin sheaths stain well by Weigert to the edge of the lesions, but show fatty changes in Marchi preparations, for a short radius round about. Prominent in these lesions are the fat-containing and leukocyte-containing phagocytes of the type so often found in all kinds of cerebral lesions. The accumulation of these was in no other case so massive as in Case I.; but they are omnipresent. Their frequency and distribution are such that many foci of these lesions look, in accordance with our usual ideas, to be of long standing.

Experimental Material. As supplement to the histological work on the lesions in man, a series of inoculations of the staphylococcus aureus was made in guinea-pigs and rabbits. Several strains of staphylococci were used, derived from various lesions, including the focus in Case VI. It was found best to employ one species of animal for serial work; and the guinea-pig was chosen. It is easy to include in single sections meninges, substance, and ventricle of the guinea-pig brain. Several methods of inoculation were employed, as beneath the skin, into the lung, through the ear-plate, and beneath the dura. The guinea-pigs stood the inoculations well and,

after recovery from chloroform anæsthesia, as a rule showed no sign of disease up to the time of examination. In some cases they were overwhelmed by the septicæmia. The fatal results are apparently more a matter of individual pig than of culture. The most convenient method was found to be the method by intrapulmonary injection.

By intrapulmonary injection of 0.5+ c.c. of a twenty-four-hour bouillon culture of the staphylococcus of the strains used one is almost certain to produce exudation into the meninges of the guinea-pig. Of this there will probably be no clinical evidence. But examination of the brains of the pigs at suitable intervals will show lesions of fairly rapid evolution. These inoculations have been controlled by subdural inoculations, with examination at similar intervals.

As early as six hours after intrapulmonary inoculation the meninges may show evidence of diapedesis of blood and exudation of polynuclear leukocytes of quite focal character. The ependyma remains clear, and no changes can be detected in the brain substance.

By twelve to fourteen hours after inoculation exudation through the ependyma is likely to be well under way.

Twenty-four hours after inoculation the vessels are injected, and blood and occasional polynuclear leukocytes are likely to be found in the pial meshes. The chief sign of inflammation, however, is the frequent demonstration in the vessels of a row or thin lining of leukocytes in the inert layer.

In one instance after intrapulmonary injection the guinea-pig immediately became paraplegic and was killed after twenty-four hours. The brain showed ependymitis, very marked meningitis, and the most extensive exudation of leukocytes into the brain substance which we were able to procure in the intrapulmonary inoculations. In this case leukocytes were very frequently seen in juxtaposition with the small pyramidal nerve cells. The same phenomenon was found later in the intrapulmonary series (although never so markedly as in this case) and is focally present in several instances in cases of subdural inoculations examined after two or three days. It is perhaps not necessary, in accounting for this occurrence of leukocytes near nerve cells, to invoke a richer lymph system for the guinea-pig brain than for the human brain. Possibly the leukocyte can more easily wander through the substance of the guinea-pig brain because it is less densely fibrillar than that of man.

Forty-eight hours after inoculation, the emigration of leukocytes into the tissue beneath the ependyma is already marked, and numerous examples can be found of leukocytes in apposition with nerve cells.

The cases examined three days after inoculation show meningitis, encephalitis, and ependymitis at their height. The controls by subdural inoculation show far more intense diffuse processes. The

three-day subdural material can be recommended for study of the cells in the lesions produced by this organism.

In material examined four and five days after inoculation the exudate is already altered by the appearance of fairly numerous cells of the lymphocyte series and a number of cells phagocytic for cell detritus.

Six days after inoculation the lesions found are meningitis and pyocephalus, due largely to exudation from the choroid plexuses. The cells found are chiefly of the polynuclear amphophile type. Mononuclear cells phagocytic for leukocytes occur. The meningitis is rarely so voluminous as the ependymitis. Numerous polynuclear leukocytes follow the cortical vessels; and it is not unusual to find leukocytes of the amphophile type in close apposition to nerve cells, as well as free in the tissue of the upper cortical layers.

The brain of the guinea-pig nine days after inoculation shows little exudative process except about certain vessels, where rare polynuclear leukocytes occur with fairly numerous cells of the mononuclear series. Occasional cells phagocytic for chromatic material occur, besides a few pigment-bearing cells. The exudate is, as a whole, slight.

Few traces of inflammation are demonstrable in the brain of a guinea-pig one month after inoculation. The brain substance shows no alteration beyond a few areas of chromophilic nerve cells mentioned below. Neuroglia fibrillæ are demonstrable beneath the pia, but in quantity which is within the normal limits for the guinea-pig by the methods used. The ependyma shows no change. The pia mater contains a few pigment-bearing phagocytes, a few lymphoid and plasma cells, and relatively many eosinophilic polynuclear leukocytes.

The examinations were throughout controlled by cultures from various organs, the brain, and the site of operation in the subdural inoculations. A surprising proportion of negative cultures was obtained from the brain even where lesions of the appropriate age could be determined. The tenuity of the lesion makes searing risky. Perhaps cultures from the ventricle are preferable in cases where the process has reached the ventricle. The above descriptions have been founded on cases in which the bacterial diagnosis was secure. The organs of the trunk were examined in many cases to make sure of the pyæmia.

Mention may be made of a frequent lesion in the guinea-pig brain which remains obscure. To be distinguished sharply from the focal occurrence of condensed, deeply staining nerve cells, and from the occurrence in compressed material and at the edges of some sections of groups of similar cells which are more or less clearly a product of technical error, are certain foci of contracted, angular or subangular, deeply staining nerve cells of the cortex. In one case there were deposited in the cell bodies of one of these chromophilic

foci dots staining by the phosphotungstic-hæmatein method. These foci of chromophilic cells occur, as far as we have yet found, without definite relation to the bacterial inoculations, but are not characteristic of the brain of normal pigs. The process is a little more frequent in groups of Purkinje cells.

RESUME. 1. The staphylococcus pyogenes aureus produces in the meninges and brain substance of man a type of inflammation in which hemorrhage is prominent.

The picture post-mortem in man varies from red softening or multiple ecchymosis and small abscess to frank and sometimes voluminous hemorrhage. The site of election for the hemorrhagic lesions is the subcortical region, supplied by the long or medullary branches of the cortical vascular system.

The histological picture varies from diapedesis and slight leukocyte emigration to abscess and acutely destructive hemorrhage with phagocytosis. Collections of mononuclear cells phagocytic for cells and cell detritus often quite obscure the acute inflammatory appearance of the lesion.

Six fatal cases in man were examined, all but one cases of general infection with the staphylococcus aureus.

A history of antecedent disease was the rule. The syndromes, which were chiefly of sudden onset and rapid course (three to fifteen days), were pyæmic, meningitic, or cerebral in type. The cases of slower course were the most plainly cerebral.

2. The staphylococcus pyogenes aureus produces in the brains of guinea-pigs an inflammatory process which tends to subside within a limited period (two weeks), and, as a rule, remains without clinical signs throughout.

No hemorrhages other than miliary perivascular ones were observed in the guinea-pig. The lesions are seldom grossly evident.

The cell pictures are of meningitis (discernible in six hours), ependymitis (twelve to fourteen hours), and exudation into the brain substance (twenty-four to forty-eight hours).

The four and five day cases show numerous cells of the lymphocyte series as well as mononuclear cells phagocytic for exudative cells. Examples of such phagocytic cells have been found as early as twenty-four hours after inoculation.

The exudation into the meninges is discernible earlier, and its traces are demonstrable later, than are the processes in the ependyma and the encephalon; but the meningitis is never so extensive or striking a process as the encephalitis or the choroiditis.

In two weeks to a month there is little sign of the previous infection.

3. The staphylococcus pyogenes aureus, of the strains and in the doses experimentally used, produces in the guinea-pig a curable encephalitis, that is a process which in logic is termed reversible. The same organism produced in our human cases extensive

brain lesions which surely look as a group irreparable. Perhaps, however, there are in man also certain cases of encephalitis which reverse themselves, and which in their course are taxed with being "functional" diseases and furnish "functional" symptoms during and after tissue repair.

We wish to thank Drs. Mason, Shattuck, Sears, and Coolidge for the use of their clinical records, and Drs. Brinckerhoff, Thompson, and Wolbach for the anatomical data in their autopsies. Drs. Councilman and Mallory have looked over the histopathological work, and Dr. W. N. Bullard has interested himself in its neurological aspect. The work was done under the Bullard Gift to the pathological department of the Harvard Medical School for 1904.

PRIMARY SPLENOMEGALY—GAUCHER TYPE.*

REPORT ON ONE OF FOUR CASES OCCURRING IN A SINGLE GENERATION OF ONE FAMILY.

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Clinical (Dr. N. E. Brill). Under the caption of primary splenomegaly have been heaped together indiscriminately a large variety of non-leukæmic enlargements of the spleen developing with or without anæmia. Osler, in an attempt to establish order out of chaos, suggested calling the cases of enlarged spleen associated with an anæmia of the chlorotic type and with hemorrhages, but unaccompanied by a leukocytosis, splenic anæmia, adopting as the cognomen the term first used by Griesinger for the splenic variety of Hodgkin's disease. He insists that these cases in their evolution present a terminal stage characterized by secondary cirrhosis of the liver associated with jaundice and ascites, which Banti described as constituting a disease *sui generis*, and which cases have been known as those of Banti's disease. But even with Osler's limitation, under the term of splenic anæmia, there have been associated diverse splenic enlargements, differing both in their clinical and pathological conditions, such as the cases described by Sippy,[1] Osler,[2] Rol-

* An abstract of this report was presented at a meeting of the New York Pathological Society on December 14, 1904.

leston,[3] Taylor,[4] Gilbert and Fournier,[5] Stengel,[6] and others. Much more work will have to be done, many more clinical and pathological investigations will have to be made, before a satisfactory classification of the varieties of types of so-called splenic anæmia can be agreed upon.

The writer insists that the type of splenomegaly first described in 1882 by Gaucher[7] as "Splenomegalie Primitive—Primary Epithelioma of the Speen," and after him by Picou and Raymond,[8] Collier,[9] and Bovaird,[10] ought not to be included in the category of splenic anæmia, because its pathology is unique and typical and the clinical picture so distinctive that it can be recognized during life. It was from the clinical picture presented by the patients whose histories I reported in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for April, 1901, that I was able to predict that my cases* belonged only to the class described by Gaucher as splenomegalie primitive. Indeed, one of the distinctive features of this class, which alone might separate it from all the cases belonging to the category of splenic anæmia is the enormous increase in the size of the liver, which almost equals the colossal size of the spleen.

For the benefit of those who have not access to the original article, a *résumé* of the clinical data of the case which forms the topic of this report is herewith given; for full details the reader is referred to the original publication. It is the first male case ever reported in literature:

Maximilian R., born in 1870, had suffered from the common infectious diseases of childhood, but never had malaria, rheumatism, or tuberculosis. He had not been rachitic and never contracted gonorrhœa or syphilis. After his ninth year he was a sturdy, muscular, healthy chap, and never was ill outside of an occasional attack of bronchitis. The only features of an abnormal nature which the patient himself observed was a tendency to sweat easily, the frequent presence of sudamina, even in winter, and a persistent patch of erythematous papules which extended from the malar prominence of one side across the skin covering the nasal bone to the same prominence on the other side, most intense, however, on the bridge of the nose. The latter developed about his fourteenth year, and, notwithstanding treatment by skin specialists, was persistent. In 1885, when he came under my observation, this patch was prominent. No signs of splenic enlargement appeared until 1889. Patient felt in perfect health all the years since his ninth. There were no pains in the splenic region at any time up to the date of the detection of an enlarged spleen. Since 1889, after an apparent initial slight reduction in the size of the spleen, there had been a steady, slow, progressive increase in size of that organ, with occasional attacks of epistaxis. In 1899 the first absolute signs of liver enlargement

* The disease has since been discovered by me in another sister, who constitutes the fourth member of the one generation of the family thus afflicted.

became demonstrable, and about this time was noticed a peculiar hard, pale, ochre-colored, wedge-shaped infiltration of the sclerotic of the nasal side of each eye, the base being limited by the cornea, the apex extending toward the nasal angle, thus differing from the ordinary pinguecula.

While feeling in perfect health the patient was losing weight very slowly but progressively. Between 1899 and 1900 the skin of the face, neck, and hands began to assume a dusky, light yellowish-brown tint. Wherever the skin was not exposed to the light and air it was perfectly normal in color. There was an entire absence of jaundice; examination of the blood and urine showed no bile.

Frequent blood examinations were made, blood counts dating from 1893, and showing a normal red and white count, and normal proportions of polynuclear neutrophiles, small and large mononuclears and eosinophiles. The hæmoglobin up to 1900 was never lower than 80 per cent. by Gowers' instrument.

The progress of the disease became rapid from August, 1900, when the patient was seized by an attack of acute colitis, starting with a chill, and followed by hyperpyrexia and diarrhœa, the movements finally becoming bloody and composed then of mucus and sanguineous fluid. Immediately after convalescence hemorrhagic furuncles appeared on the legs, thighs, trunk, arms, and forehead, leaving behind them, when healed, permanent pigmented spots at the site of each furuncle. Excepting these spots and the peculiar change in color of the face and hands, there was no pigmentation anywhere of the skin or of the mucous membranes accessible to inspection. Later in the year the first signs of petechiæ appeared, three on the thorax.

From January, 1902, to May, 1902, there was very little if any change in the condition of the patient. In May he began to complain of pain in the lower end of the left tibia. Physical examination at the seat of pain revealed nothing, there being no swelling, redness, or tenderness.

On June 6, 1902, he was seized by an attack of malarial infection, with the usual signs of the tertian type; plasmodia were found in the blood. A course of quinine dissipated the organisms. Epistaxis, which had not been frequent in the past, now became more so, and the blood examinations revealed a steady decrease in hæmoglobin to 45 per cent., and a slight increase in leukocytes, 8240; the red cells being diminished, 3,420,000. The red cells showed a few normoblasts (August 1, 1902). He complained less of pain in the lower part of the tibia; occasionally this pain disappeared entirely, even for a month at a time. During the attack of malarial infection there was no demonstrable increase in the size of the spleen.

In September the patient was so well that he again attended actively to business. He remained in a condition of relative well-being throughout the rest of the year and the first half of the follow-

ing year, 1903. During these nine months he had but four attacks of epistaxis. In April, 1903, he began to complain again of the pain in the neighborhood of the ankle and also about the left knee. There were no local signs of swelling, etc., and no indications of a hæmarthrosis. A blood examination at this date revealed the following: red cells, 4,400,000; white, 5240; hæmoglobin, 55 per cent.; polynuclear neutrophiles, 65 per cent.; small mononuclear, 26.5 per cent.; large mononuclear, 6.5 per cent.; transitional forms, 1 per cent.; eosinophiles, 0.5 per cent.

In June, 1903, in the warm spell, his sudamina became pronounced, a few miliaria becoming hemorrhagic; the erythematous patch on the nose became more livid. The pain in the left knee and ankle, however, disappeared. The heated term weakened him considerably, and he left town, spending the next three months in the mountains, where he felt very well.

On his return examination revealed a slight increase in the size of the spleen, its anterior border extending 3 cm. beyond the middle line; the upper border (dulness) was at the fifth rib in the midaxillary line; the posterior border could be felt in a line with the angle of the scapula about 4 cm. from the lumbar spines, and became lost to the touch behind the iliac crest. The liver had relatively increased more in size. Liver flatness was elicited at the fourth rib, lower border palpable 4 cm. below the level of the umbilicus, extending below the iliac crest in the midaxillary and postaxillary lines. His chest and abdomen were more bulging than ever.

September 27, 1903. Red cells, 4,200,000; white cells, 6200; polynuclears, 70 per cent.; small lymphocytes, 22 per cent.; large lymphocytes and transitionals, 7 per cent.; eosinophiles, 0.5 per cent.

Heart. Loud systolic murmur at apex and over pulmonary area; upper border of cardiac dulness at lower border of second rib; right border at right sternal line; apex in third interspace.

November 17*th*. A moderately severe epistaxis.

27*th*. A few petechiæ are noted on the dorsum of each hand; none on conjunctivæ. Hæmoglobin, 50 per cent. Patient has a ravenous appetite. Again complains of pain in left knee and ankle. He, however, has been taking long walks daily. No demonstrable increase in size of spleen or liver.

January 6, 1904. First appearance of ecchymosis—one ecchymotic spot on left lower leg near the end of the fibula and one on dorsum of left foot, each about 2 cm. in diameter. Emaciation much more marked since last note. Hæmic murmur increased in intensity. Hæmoglobin, 45 per cent. No epistaxis since November 17, 1903, yet a gradual hæmoglobin reduction. No ascites. Has had dyspeptic symptoms, perhaps partly due to the excessive amount of food he has been taking.

March 12*th*. Patient began to complain of dyspnœa and fever, with great weakness. Temperature, 101°. Limit of cardiac dulness

considerably to right of sternum; left border not definable, owing to interference of spleen; apex beat feeble and in third interspace. Same hæmic murmur. No recognizable increase in spleen and liver.

13*th*. Patient feeling better. Temperature, 100°; two ecchymotic (fresh) spots over right tibia; another on dorsum of left foot. Dyspnœa; respirations, 34. Says he feels comfortable.

20*th*. Since last note normal temperature until yesterday. To-day increased difficulty in breathing, pain behind sternum, sticking and rubbing in character; chills; respiration 38 and labored; pulse 116; temperature 103°. Apex beat cannot be felt; to-and-fro superficial friction at junction of third right rib with sternum. Diagnosis of pericarditis, with probable bloody effusion. From this day on fever persisted, weakness became extreme, the patient became irritable, objected to further blood examinations. Signs of fluid in peritoneal cavity. Dyspnœa more extreme, the pericardial friction more rough and superficial, the pulse became weaker; exitus, with mental faculties preserved to final moment, on March 30, 1904.

Negative Symptoms. Urine never contained bile; negative examination for pathological urobilin (Jaffé); never any casts; never albumin; urea never much above normal limits; highest 3.4 per cent. Ascites never present, except two days before death. Œdema absent. Jaundice absent throughout. Superficial lymph nodes never enlarged.

Blood. Never contained bile; coagulation time gradually increased in length toward terminal stage of disease to fourteen minutes, first examination in 1899 being three minutes.

Hemorrhages. Epistaxis was the only form. The attack of colitis associated with bloody stools cannot be considered as a melæna. Toward the last two years of life petechiæ and ecchymosis, few, however, in number.

Discoloration of Skin. Limited to face and neck, wrist and hands. Skin of body not discolored. Discoloration not that of Addison's disease; color, yellowish-brown. It would appear as if the light and air had some influence in changing the tint of the exposed parts. The color is not one due to ordinary exposure; it remained permanent. Bovaird mentions bronzing of the face and hands of his patient. Bronzing is not applicable to this case.

Local pain over spleen and liver absent, though such could be elicited by pressure.

No bone tenderness; pressure over lower end of femur and tibia relieved the pain when present in those regions.

No feeling of being sick except during an intercurrent affection—colitis, malarial disease, terminal pericarditis—on the contrary, a feeling of well-being.

Owing to the unusual importance of this case, I have been happy to call into its collaboration the aid of Dr. Mandlebaum, who made

the histological examination and who prepared the photomicrographs, and of Dr. Libman, who made the autopsy.

REPORT ON POST-MORTEM EXAMINATION MADE MARCH 31, 1904, 11.45 P.M.—No rigor mortis; body emaciated; pupils large; yellowish-brown discoloration of face and hands. A few small lymph nodes in both axillæ the size of peas; in supraclavicular regions a few half the size; the same in the epitrochlear and inguinal regions. Panniculus adiposus atrophic; muscles of the abdominal wall succulent. In the abdomen 1000 c.c. of hemorrhagic fluid, chocolate in color. The body musculature is atrophic, pale.

Old and recent adhesions over liver; omentum adherent to anterior surface of the spleen; the spleen at its upper pole is adherent to the surrounding tissues.

Diaphragm on the right side at the third rib and on the left at the fourth rib. Lower part of the chest markedly expanded. All the intra-abdominal veins are distended.

Anterior mediastinal nodes enlarged the size of peas, yellowish-brown in color; on section there are pinpoint hemorrhagic areas.

Lungs. No fluid in pleural sacs; both lungs congested, lower lobes compressed. Lingula emphysematous. Bronchial nodes moderately enlarged and anthracotic.

Pericardium. Very markedly distended by 2 litres of very bloody fluid. Microscopic examination of the fluid reveals altered erythrocytes only. The visceral pericardium is coated by a layer of shaggy fibrin, which is easily removed.

Heart. Small; old thickening of posterior visceral pericardium; right auricle dilated. Tricuspid orifice admits three fingers; the valve is slightly thickened. The wall of the right ventricle is thin. The pulmonary valves are negative. The left ventricle is small; the auricle dilated. The heart muscle is firm, brownish. The coronaries and aorta show no lesions. There are no congenital defects.

Œsophagus and Stomach. Marked congestion. Stomach is dilated.

Spleen. Immensely enlarged, filling the larger part of the abdominal cavity. The weight is 5280 g. (11 pounds). It measures 40 x 20 x 14 cm. The organ is of an elongated ovoid form. The surface as a whole is of a reddish-brown color and shows marked recent and old perisplenitis. There are irregular depressed areas on the surface, evidently the result of infarctions. The organ is very firm. On section the color is that of chocolate, but here and there are lighter areas of a grayish-red color. The pulp is moderately swollen. There is a large number of old and recent infarctions, mostly peripheral. In some sections the whole periphery is made up of infarcted tissue; some of these infarcts are surrounded by hemorrhagic zones; most are anæmic and look cheesy. In the lower pole there is a white area about 1.5 cm. wide, crossing the entire width of the spleen. Where the pulp is less swollen the con-

nective tissue is seen to be decidedly increased. In the pulp are a number of small hemorrhages. The splenic vessels show no changes. At the lower part there is a globular mass of splenic tissue attached by a flat pedicle to the main organ; it measures 4 x 6 cm. On section it is dark brown in color, with grayish markings.

Liver. Weight 4.8 k. (10 pounds). It measures 35 cm. in width; both lobes are 27 cm. in length; thickness of the organ is 13 cm. There is marked old and recent perihepatitis. The surface is pale reddish-brown, with irregular white and dark-brown markings. The right lobe is oblong; the left ovoid; the free border is rounded. On section the organ is quite firm. As a whole it is chocolate-colored; the cut surface is rather granular. Throughout the liver are irregular white markings, varying in diameter from 0.5 cm. to 2 or 3 cm., which, for the most part, are ramifying. They do not seem to bear any definite relation to the lobular markings. In both lobes, but especially in the right, there is a number of fine hemorrhages. The portal vein and the gall-ducts show no changes. The gall-bladder is distended by a large amount of very dark bile. The wall appears to be normal.

Kidneys. Left: weight, 150 g., capsule markedly adherent; moderate lobulation; surface slightly granular; veins injected. On section the organ is quite firm. The cortex is narrow, but swollen; the markings are poor. There is a hemorrhagic area in the labyrinth. There are uric acid deposits in the cortex and in the papillæ; also lime infarctions in the latter. In the pelvis there are petechiæ and one large hemorrhage. Right: weight, 120 g.; surface the same as that of the left kidney; cortex, yellow in color. The organ is succulent; there are hemorrhages in the pelvis. Just external to the pelvis there is a border of very succulent, reddish tissue, varying in width from 0.5 cm. to 1 cm. There are uric acid and lime deposits as in the left kidney.

Ureters. Negative.

Adrenals. Negative.

Pancreas. Negative.

Small Intestine. The walls of the jejunum and duodenum show blood injection; the contents are tarry. The mucosa of the ileum is swollen, and there are hemorrhages in the wall.

Colon. Small effusion of blood in and under the mucosa of the ileocæcal valve and the cæcum. The contents of the large intestine are hemorrhagic. No evidences of lymphatic hyperplasia. The wall of the rectum is injected.

Bladder. Marked injection of the vessels of the trigone. Prostate normal in size; color, yellowish.

Lymph Nodes. The mesenteric nodes moderately enlarged; they look like the prevertebral nodes. The latter vary in size, the largest being about the size of a large bean. They are fairly soft, ochre in color, and show some hemorrhagic markings.

Bone-marrow of Femur. Uniformly dark red in color; quite firm; no changes in bone.

Thoracic duct is formed by two separate channels, which coalesce just below the diaphragm.

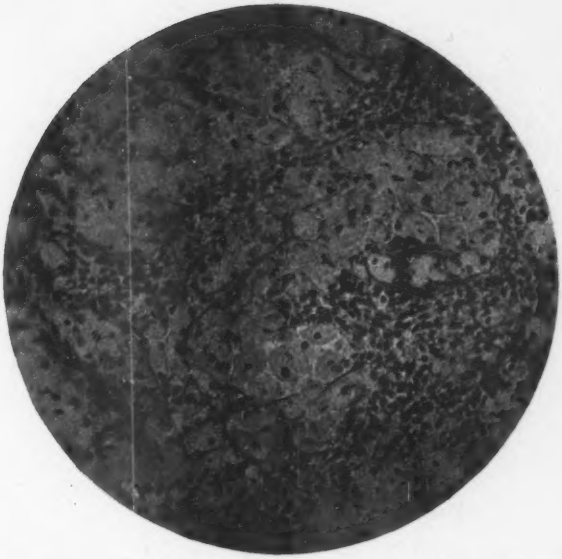
Bacteriological Examination. Cultures made from the heart blood remain sterile. Those made from the spleen show the staphylococcus albus.

MICROSCOPIC FINDINGS. Pieces of tissue from various parts of the organs were fixed in Zenker's solution, saturated sublimate, formalin, alcohol, Müller's fluid, and Orth's solution, and were embedded both in celloidin and paraffin. The ordinary histological stains were employed, also iron hæmatoxylin, Biondi-Heidenhain, Pappenheim's methyl-green pyronin, Mallory's connective-tissue stain, Unna's polychrome methylene blue, Weigert's modified Van Gieson's stain, and others.

Spleen. Certain peculiarities are found in sections from different parts of the organ. Many dense bands of fibrous connective tissue are seen surrounding certain parts of the splenic tissue. In places where these bands are less dense, the individual connective-tissue fibres are seen to be slightly separated from one another by a faintly staining homogeneous substance containing a few mononuclear cells and giving the usual appearances of œdema. Occasionally an area is found near the margin of a band of connective tissue, where the fibres are more widely separated, giving rise to small, irregularly shaped spaces or meshes. As a rule, these spaces contain a few normal pulp cells, though here and there an endothelial cell of the type described below is seen, entirely surrounded by delicate connective-tissue fibres. The capsule and the trabecular arrangement are quite normal, with the exception of certain pigment, which will be mentioned below, and a slight increase in the amount of connective tissue. The infarcts are of the usual anæmic variety. Some of these contain areas of necrosis, with many slit-like openings, due, in all probability, to the presence of cholesterin crystals. In some of the necrotic areas the remnants of alveolar spaces filled with endothelial cells, as described below, can be seen.

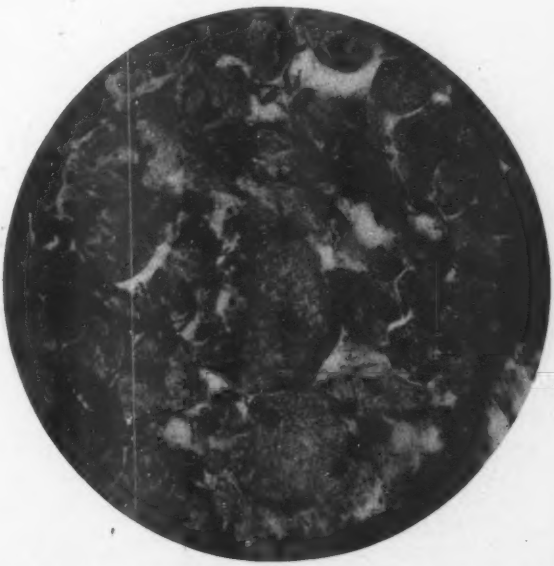
Scattered throughout all the sections are large masses of cells which require further description and which seem to be the principal and characteristic feature of the disease. The cells are found mainly in large, irregularly shaped, alveolar spaces, whose walls are composed of delicate connective tissue lined by endothelium. Fine capillaries are seen in the walls in places where the latter are somewhat thickened. These alveolar spaces measure from 130μ by 269μ to 95μ by 108μ, respectively. Many variations in size occur between these extremes. The alveolar spaces or pulp spaces may be looked upon, according to Weidenreich,[11] as the venous capillaries of the spleen. In some places a direct connection between adjacent alveoli is found to exist.

FIG. 1.



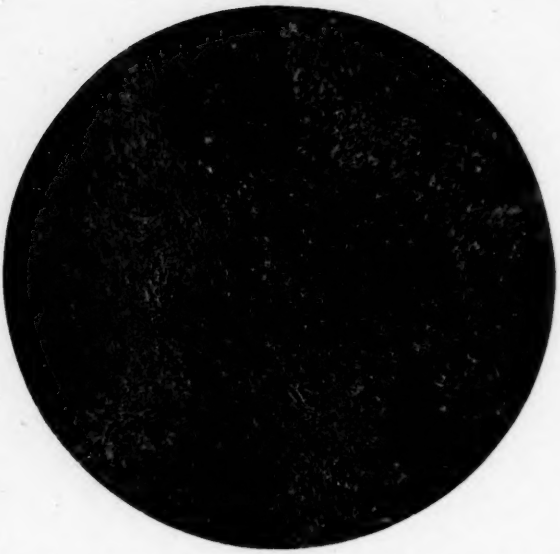
Photomicrograph of spleen, showing the alveoli filled with endothelial cells. × 250.

FIG. 2.



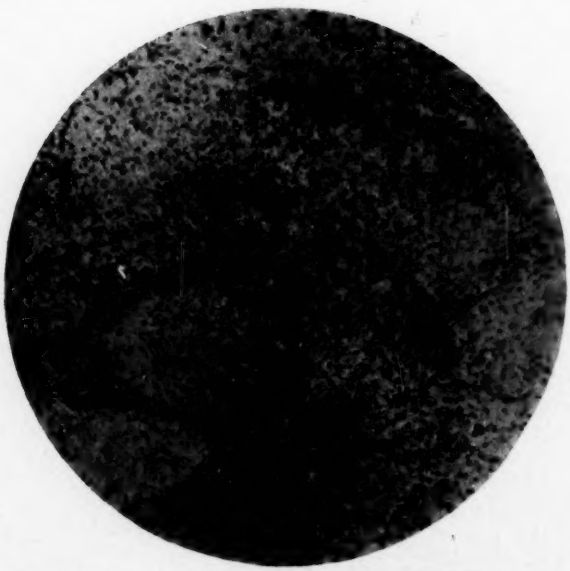
Photomicrograph, showing the general granular and streaked appearance of the endothelial cells. × 500

FIG. 3.



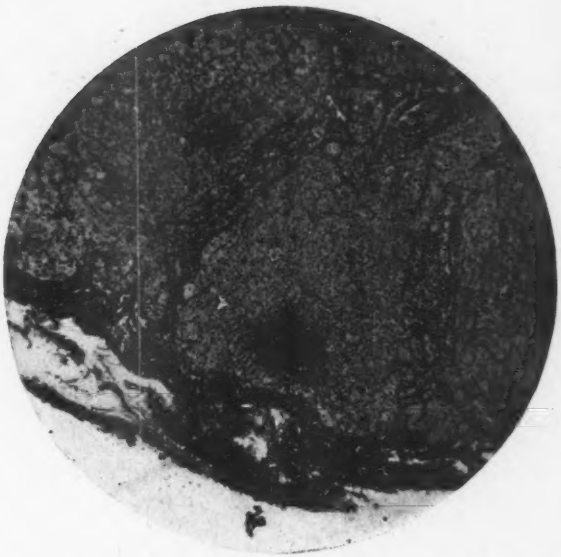
Photomicrograph of liver, low power, showing the increase in connective tissue and the general appearance of diffuse cirrhosis.

FIG. 4.



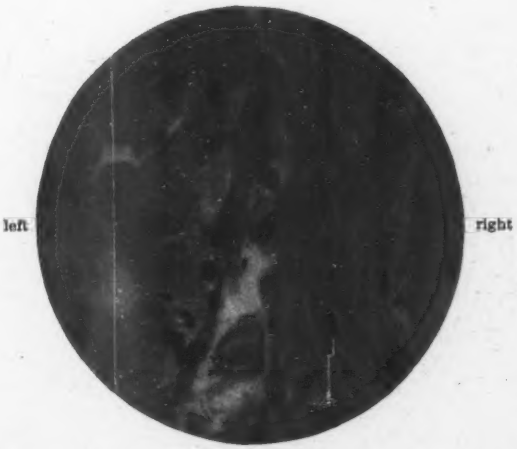
Photomicrograph of lymph node, showing the pigment distribution and the endothelial hyperplasia. × 125.

FIG. 5.



Photomicrograph of lymph node, low power, showing remnants of two follicles and absence of normal lymphoid tissue.

FIG. 6.



Photomicrograph of lymph sinus containing pigment granules and endothelial cells in its lumen. On the right is the connective tissue of the capsule; on the left are endothelial cells arising from the wall. × 500.

FIG. 7.

Photomicrograph of lymph node, showing the endothelial cells arising from the reticulum, and the general type of the multinuclear endothelial cells. × 250.

FIG. 8.

Photomicrograph of bone-marrow, showing a small group of endothelial cells. × 250.

The endothelial cells which line these spaces can readily be seen. In some places they are of normal appearance; in other places they are distinctly swollen. Occasionally a few very delicate connective-tissue fibres may be found within the alveoli. The endothelial cells filling these spaces are so abundant in number that in many places it is impossible to distinguish any of the normal splenic tissue. Only here and there can a single Malpighian body be seen. These bodies have no degenerative changes, but the central artery shows a slight thickening of its walls. Here and there a few connective-tissue fibres can be found in the Malpighian bodies themselves, principally at the periphery. The cells are found both lying free and attached to the wall of the spaces, and their size and shape corresponds to the amount of pressure exerted upon them. For the most part, the cells resemble swollen endothelial cells. They are, as a rule, quite large in size, round, oval, or polygonal in shape, depending upon the number in a given space (Fig. 1). The cell bodies stain faintly, but distinctly with eosin or picric acid, and show a slightly granular appearance of the cytoplasm, but no degenerative changes. The outline of the cell body is usually well preserved. In thin paraffin sections a distinct network of fine linear markings can be seen in some of the cells; with the high power these fine lines seem to be composed of minute dots. In other cells very delicate wavy lines are distinguished, arranged in a more or less concentric form, giving a streaked or wrinkled appearance to the cell. This appearance of the cytoplasm is well brought out by Mallory's phosphomolybdic acid hæmatoxylin stain. Fig. 2 shows the general granular and streaked appearance of the cells under high amplification. Vacuoles are not uncommon, as many as four or five being present in some of the larger cells. In favorable parts of the sections the cells can be seen arising directly from the endothelial lining of the pulp spaces, or, more properly, venous capillaries. In size the cells vary from 17.4μ by 21.75μ, to 34.8μ by 47.85μ, respectively. Nuclei of a relatively small size are seen in the cells. The average measurement is 5.43μ by 8.7μ. These are found either centrally placed or near the periphery. Some of the cells contain three or four nuclei, but the number of nuclei found in a single cell does not correspond always to the size of the latter, for some of the very largest cells contain but a single nucleus. The nuclei vary considerably in size, from small, round, deeply staining bodies rich in chromatin, to larger, irregular forms staining rather freely. Some of the nuclei show atypical mitotic changes, and a few contain distinct nucleoli. No typical giant cells are seen in any of the sections. Here and there the pulp spaces are seen well distended with red blood cells and normal adenoid tissues. Some of these spaces contain but a few endothelial cells; others show a relatively large number. Many of the bloodvessels throughout the sections are surrounded by a slight increase of connective tissue. A few veins, however,

are noted, whose walls appear quite normal. These are filled with blood.

Light, brownish-colored pigment particles are scattered here and there in the pulp spaces and also in some of the pulp cells. Throughout the trabeculæ fine granules of brownish-yellow pigment are seen, in long spindle-form arrangement, corresponding to the capillaries and also lying free between the connective-tissue fibres. Sections treated with potassium ferrocyanide and hydrochloric acid give the characteristic iron reaction. Sections were stained for bacteria, but none could be discovered. Neither could any bodies be found resembling protozoa.

Liver. The capsule is much thickened and contains many pigment granules. A striking feature in all the sections is the enormous increase in the amount of interlobular connective tissue throughout the organ, without any apparent influence upon the liver cells themselves. This interlobular structure is composed of very delicate connective-tissue fibres containing numerous capillaries and some pigment. With Mallory's aniline-blue stain a few very fine fibrillæ can be seen extending into the lobules here and there. The bile-ducts are not increased in number and appear quite normal. Under the low power the general picture is that of a diffuse hepatic cirrhosis (Fig. 3). The liver cells, for the most part, are normal, though occasionally a cell is seen containing minute fat-droplets, and a few nuclei show the usual appearance of regeneration.

The peculiar endothelial cells described in the spleen are also found in abundance in this organ. A few are seen in the lobule proper, but the majority are situated in interlobular connective-tissue spaces. In the lobules these cells are, for the most part, situated in the capillaries at the periphery, though now and then single cells can be found in the deeper parts of the lobule surrounded by liver cells. The individual endothelial cells can be made out quite readily, though they are not so clearly defined as in the spleen. In the interlobular connective-tissue spaces the cells are so intimately fused together that their recognition is somewhat more difficult, but sections treated by Weigert's modified Van Gieson's stain show the cell bodies quite distinctly. In every other respect the cells are identical in appearance with those found in the spleen. In a few places there seems to be a tendency for these cells to invade the lobule itself, but, for the most part, the cells seem to be confined to these spaces and in intimate union with the connective-tissue fibres. The pigment in this organ responds also to the test for hæmosiderin. The bloodvessels appear quite normal, as a rule. Some of the arteries have slightly thickened walls.

Mesenteric Lymph Nodes. The capsule and trabeculæ are sharply defined by the large amount of pigment which outlines their course. Throughout the nodes the trabeculæ are deeply pigmented, but not otherwise affected (Fig. 4). The pigment is dark brown in

color, and in the thinnest sections can be seen either as elongated whetstone-shaped crystals or as fine amorphous particles. Smaller masses of pigment are also seen distributed in the cortical and medullary portions of the node. The lymph sinuses are all filled with pigment. Iron reaction is present. The nodes are so changed in general appearance and structure that the usual characteristics have entirely disappeared. A section through the central portion of a somewhat enlarged node shows less than ten follicles. The germinal centres are not well marked, but otherwise the follicles are quite normal, excepting that occasionally a few delicate connective-tissue fibres may be seen in the follicle near its periphery. Only here and there are small remnants of normal lymphoid tissue seen (Fig. 5). The medullary portion of the node is somewhat less affected than the cortical substance. The reticulum of the organ is well preserved.

The entire node is practically transformed by the presence of endothelial cells, such as were described in the spleen and liver. With the exception of the connective-tissue structures, follicles, and small remnants of lymphoid tissue, the whole section is but one mass of these cells. Notwithstanding this fact, the individual cells are most distinctly outlined and clearly seen and show but a slight tendency to fuse together. The cells can be seen arising from the walls of the lymph sinuses (Fig. 6), and from the reticulum throughout the node (Fig. 7). In size, shape, structure, and staining properties, the cells are identical with those described above. A few very large cells measuring 39.15μ by 56.55μ, are present. Some contain as many as nine nuclei. These are not arranged in any particular form, and no cells are found presenting any of the usual appearances of giant cells. The bloodvessels are surrounded by a slightly increased amount of connective tissue, but show no other changes.

Bronchial Lymph Nodes. These nodes are affected in a like manner. The endothelial cells are of the same general structure and appearance as in the mesenteric lymph nodes and distributed in a similar manner, but they are not present in such great numbers. Here and there small areas of quite normal adenoid tissue are seen, with fairly well-preserved follicles. Pigment is also present and is identical in color, distribution, and reaction with that found in the mesenteric nodes. Besides this, a moderate amount of anthracosis is present. The capsule and trabeculæ show a rather marked increase in amount of connective tissue. The bloodvessels are prominent throughout and well distended with blood. Their walls are somewhat thickened, but show no degenerative changes.

Retroperitoneal Lymph Nodes. The same process is also found here. The general picture is identical, but a few slight differences may be noted. The capsule is more markedly thickened than in the other nodes, but the pigment, particularly in the lymph sinuses, is not as prominent. Surrounding the follicles are quite a number

of small capillaries, and the margins of the follicles show the presence of young connective-tissue fibres. Numerous small bloodvessels, mostly arteries, are seen. These vessels show hyaline changes. In parts of the section degenerative processes have occurred, so that many of the endothelial cells, as well as the adenoid tissue, do not stain distinctly. The entire process in these nodes seems somewhat older than in those described above.

Bone-marrow. Cells identical with those in the above-described organs are found in abundance in the bone-marrow. There is considerable variation in the size of the cells in the bone-marrow as compared with those found in the other organs, but the general characteristics are preserved. Vacuoles are common in these cells. No forms are found with an excessive number of nuclei, neither are any of the very large types, such as were described in the lymph nodes, to be seen. Occasionally a large mass of these cells is noted, but for the greater part they are found either singly or in groups of from four to ten cells (Fig. 8). In the latter instance the cells are always found in intimate relationship with the walls of the capillaries or attached to the connective-tissue reticulum. The larger masses cannot always be seen to have such a relationship, and occasionally they are found surrounded by a considerable number of red blood cells. In a few places the cells are distinctly seen within the lumen of dilated capillaries.

A large number of stains were employed in the examination of these sections, but the Biondi-Heidenhain method gave the best results, bringing out the connective-tissue reticulum with much clearness. A few polynuclear leukocytes, some of which show eosinophile granulations, are present, also normoblasts and giant cells in considerable numbers. The larger bloodvessels appear normal. No pigment is present.

Spreads made from the bone-marrow by Dr. Libman, and stained with eosin-hæmatoxylin, Ehrlich's triacid stain, Jenner's stain, and Wright's stain, show the following: There are present many erythrocytes; these are of about the normal size or larger (macrocytes). Slight poikilocytosis is also noted. Normoblasts are very abundant, showing karyokinetic and karyolytic changes. Small and large lymphocytes and mononuclears are present; also polynuclear neutrophilic and eosinophilic leukocytes, but the main bulk of leukocytes is made up by neutrophilic and eosinophilic myelocytes. Some of these are quite large, as are also some of the polynuclear leukocytes. With the Wright stain azurophile granules are seen in a few lymphocytes. Mastzellen are not to be found. The large endothelial cells have basophilic nuclei; their cytoplasm stains slightly basophilic and faintly acidophilic. Giant cells are abundant.

The spreads of the spleen and liver show no nucleated erythrocytes, no giant cells of the type seen in the marrow, and no myelocytes. The cytoplasm of a few of the endothelial cells is granular-

looking, the granules taking on an appearance resembling neutrophilic granulations, but they do not impress one as possessing true granulations.

Lung. The vessels are all distended with blood. The vesicles are compressed in a great measure and show evidences of œdema. A moderate amount of fibroid induration is present. The sections show a moderate degree of anthracosis, and some hæmatogenous pigment is seen scattered through the organ.

Heart. The pericardium shows a recent serofibrinous exudate with the production of young connective-tissue fibres. In the meshes of this exudate are a large number of small round cells and some red blood cells. Many newly-formed capillaries are also noted. The muscle fibres of the heart show considerable parenchymatous degeneration; also a moderate amount of brown atrophy. No changes are seen in the bloodvessels.

Kidney. Sections show the usual picture of a chronic interstitial nephritis. Bowman's capsule is much thickened, and here and there the glomeruli are entirely replaced by fibrous tissue. The tubular epithelium is coarsely granular, and the nuclei are occasionally missing. The epithelium shows vacuoles in places. There is also some increase in connective tissue between the tubules, and a few areas of infiltration by small round cells are seen. The vessels are the seat of endarteritis, and the sections also show a slight amount of congestion. Small deposits of lime salts are present. The right kidney shows rather more congestion than the left, and in the medulla is a large hemorrhagic area containing blood pigment and surrounded by a zone of chronic inflammatory tissue.

Pancreas. This organ shows no lesion.

Adrenal. The sections are normal.

Colon. The mucosa is somewhat congested. In the submucosa are many dilated veins filled with blood. Otherwise the sections are quite normal.

While the study of this case was nearing completion, the sister of this patient met with a fatal accident. Her organs are now being studied. Owing to the fact that these may give additional information, we shall reserve our full discussion of the features of these cases to a subsequent publication.

We may state, however, that our findings enable us to place this case in the group described by Gaucher, Picou and Raymond, Collier, and Bovaird. The spleen and liver show the same changes as described by Gaucher, but he has not reported fully in regard to the lymph nodes. Picou and Raymond report simply on the spleen and lymph nodes, as in their case the spleen was removed at operation. Our findings correspond with theirs in nearly every respect. The spleen in Collier's case is also identical. Bovaird's case and ours are also similar, but our case is the first one in which the bone-marrow was examined and the endothelial hyperplasia discovered.

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SUCTORIAL AND OTHER INSECTS AS PLAGUE CARRIERS.

A NEW SPECIES OF RAT FLEA.

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AMONG over twenty fatal plague cases investigated by the writer there was one in which it strongly appeared that the infecting bacilli had been carried into the body of the patient—a child—by *pediculi capitis*. It is stated advisedly that this mode of infection appeared very probable, because it is naturally impossible to be certain beyond doubt as to such an occurrence. Only experimental trials on human beings could firmly establish the possibility of this mode of transmittal; but such tests with plague bacilli are of course, inadmissible.

The question whether insects, and particularly parasitic ones, play a more or less important role in the spreading of plague is still far from being settled definitely, as the views of investigators and writers upon this subject are much divided. Among the modern workers on plague who first gave their attention to insects as plague carriers is Hankin,[1] who reports that he carried out a long series of researches on the relation of rat-cadaver-eating ants to the possible spread of plague. He found that ants neither die of plague nor retain the infection for any time. By making extracts of ants shortly after they had eaten from rats dead of plague, Hankin obtained a material which, when injected into rats and mice, would kill them, producing typical plague lesions in them.

Ogata,[2] in studying a plague epidemic in Formosa, took seven fleas from a rat dead of plague, crushed them between sterile slides,

and injected the material so obtained into two mice. One of the latter died of plague, while the other one remained well.

La Bonadiere and Xanthopulides[3] showed, as they maintain, by cultural methods the presence of plague bacilli in a mosquito (moustique) which had bitten a patient sick with plague.

Simond[4] is inclined to attribute much importance to rat fleas as plague carriers. He found bacilli similar morphologically to that of plague in fleas taken from rats affected with the disease. He inoculated three mice with material obtained from such fleas, but only one of them died, the other two surviving.

Loir[5] goes so far as to see in the flea the principal intermediary carrier of plague between rat and man; but, as Galli-Valerio has pointed out, Loir has really no valid experiments to support his claim, which he, however, sees fit to bring forward as a demonstrated fact.

Kolle[6] has systematically tried to infect healthy rats from those sick with or dead of plague through the agency of fleas. He has, however, never succeeded in transmitting plague in this manner, though he was able to demonstrate that fleas had really travelled from sick rats to healthy ones. From his observations on rats he thinks that the disease spreads among these animals owing to the habit of the living to eat the cadavers of the dead of their own kind, and not through the agency of fleas passing from plague-sick to healthy individuals. The primary bubo in rats dead from plague is generally found in the submaxillary region, which points to an infection through a slight lesion in the buccal mucosa. Kolle, in speaking on the subject, very properly remarks: "It is clear that plague bacilli will enter the body of parasitic insects which suck the blood of animals sick with plague. It has, however, not yet been shown beyond a doubt that the bite of such parasites will infect other healthy animals."

Nuttall[7] made experiments to clear up the question as to what part insects play in the spread of plague. He demonstrated that when flies had been fed on material containing plague bacilli they still harbored the virulent organisms twenty-four and forty-eight hours after the last feeding. According to this author, the danger of a spread of the disease through bed-bugs is very negligible. The evidence in favor of the "flea hypothesis" as far as the spread of plague is concerned, Nuttall[7] considers worthless and unable to withstand scientific criticism. He states that all of his attempts to infect rats or mice through the bites of freshly infected fleas have proved futile.

Galli-Valerio[8 9 10] severely and justly criticises the evidence so far brought forward to show that rat fleas play the most important role in the dissemination of plague among the human inhabitants of a district infected with this disease. He particularly shows that most of those who have on very insufficient evidence assumed that

fleas from rats spread plague among human beings have not even ascertained whether the species of fleas infesting the rats will at all bite man. Galli-Valerio found *typhlopsylla musculi* and *pulex fasciatus* on European rats and mice under normal conditions. He allowed himself to be invaded by fasting individuals of these two flea species, but neither of them bit him. *Pulex serraticeps*, the flea infesting dogs and cats, and which occasionally bites man, was not found by Galli-Valerio on rats.

Tidswell,[11] who made his observations during the last plague epidemic at Sydney, reports that he collected one hundred fleas from rats, of which ten were identified as *pulex fasciatus*, eight as *typhlopsylla musculi*, one as *pulex serraticeps*, and eighty-one as *pulex pallidus*. The last one, it appears, has not previously been mentioned as occurring on ordinary rats; its stated hosts are, according to Thompson, *mus albipes* of Socotra, and *herpestes ichneumon* of Egypt. This species, the author states, bit human beings in laboratory trials, as did also *pulex fasciatus* on one occasion. *Typhlopsylla musculi* did not bite.*

Thompson,[12] who during the Sydney epidemic observed blebs which he considered to be produced by fleas and to be the place of entrance of the plague virus, concludes that the transmission of plague from rats and mice through the intermediation of fleas must be very frequent.

Zirolia[13] believes that plague can be easily spread by fleas. He observed *pulex irritans* and *pulex serraticeps*, after they had been fasting for some time, suck blood from a plague-infected mouse, and he found living, virulent plague bacilli in the body of the fleas from seven to eight days after they had partaken of the infected blood. Zirolia also says that the feces of fleas from plague-infected animals contain virulent bacilli and that these parasites survive for a long time in the bodies of dead fleas.

Maxwell,[14] from his observations made in Changpoo, China, states that he is getting to be more and more doubtful about the rat-flea theory. "I cannot see," he says, "how we can escape plague. I must have been bitten in spite of flea powder many times off plague patients, and so must my students. The Chinese, especially the women, catch the fleas and kill them with their teeth. If they catch fleas with plague bacilli in them, how do they escape?"

The Indian Plague Commission,[15] which studied plague in all of its phases in India, has also looked into the question of insects as carriers of the disease, and in its report says that Simond's endeavors to establish the proposition that suctorial insects play

* Galli-Valerio, trying to invalidate Tidswell's observations, says that this author, like others, failed to transmit plague from rat to rat through the agency of fleas, and proposes the question: "If the transmission is so difficult from rat to rat, why, on the other hand, should it be so frequent from rats and mice to man who is not, as a general rule, attacked by mouse and rat-fleas?"

an important part in the transfer of plague from sick to healthy animals is so weak as hardly to deserve consideration. The experience of plague hospitals in India, and especially that of the Arthur Road Hospital at Bombay, seems to indicate very clearly that suctorial insects do not come into consideration in connection with the spread of plague. The staff and attendants in the Arthur Road Hospital (where thousands of plague cases are treated) were continually bitten by insects, especially mosquitoes, and yet no cases of transfer of the infection from the sick to the healthy came under observation.

The Commission also states that, on reviewing all the facts which have come to its knowledge, it has little reason to suppose that ordinary, casual contact with plague-infected rats, dead or alive, is especially liable to convey the disease. On the other hand, examples are known of cases where the bite of plague-infected rats and other animals has conveyed the disease.

The report of the Commission, however, does contain some information which suggests that *pediculi* may be factors in the spread of plague. According to the Bombay* statistics of the plague epidemic of 1896, the rate of mortality per 1000 individuals among the Jains of that city as compared with the rate of mortality among the other castes in its population is surprisingly large, and it is believed to be due to the fact that animal life is sacred among the Jains. "They will not," the report says, "sweep their staircases, or sweep their sleeping-rooms, or their cooking-rooms very often, lest they should destroy some animal life, so scrupulous are they. . . . Not that their places are very dirty. They are a wealthy people, and their places look comparatively clean. . . . The Jains, owing to their aversion to taking life, are said to be infected with parasites."

A New Species of Rat Flea. There has certainly not yet been presented much evidence in favor of the theory that the most important intermediaries in spreading plague from rats to man are fleas from plague-infected rats. Even if rat fleas should have played an important role in the spread of plague in Sydney, as maintained by Tidswell and Thompson, their conclusions cannot be generalized. How necessary it is to look into this question in every place where plague occurs endemically or epidemically is shown by our observations made with reference to rat fleas in Manila. Looking into this subject we found, somewhat to our surprise, that the fleas infesting rats in Manila are not identical with those which have been described for other countries. Indeed, the species found here on rats appears to be one which has not yet been described. Previous to the time when the writer began to collect rat fleas, Dr. W. B. Wherry had already secured eight, which he kindly placed at

* Average mortality per 1000 males in the plague epidemic of 1896 at Bombay, 2.63; per 1000 females, 1.88; per 100 male Jains, 8.09; per 1000 female Jains, 6.77.

my disposal. Thirty-four more were subsequently caught. It is not easy to procure a large number of rat fleas, because, when the rodents have been caught in traps it is found that by the time they are killed and examined the fleas have left them. For this reason Dr. Wherry succeeded in obtaining eight fleas only from fifty-three rats, while thirty-four more were subsequently obtained from about one hundred rats. A few of the parasites were procured alive, were kept in a glass vessel for some time, and were then given a chance to bite both Caucasians and native Filipinos. In not a single instance did any of these fleas bite human beings. We have also collected from persons working in the laboratory, where numerous animals are kept and where a large number of rats are sent for examination for plague infection, a number of fleas which proved to be *pulex irritans* and *pulex serraticeps*. The flea occurring on rats in Manila was never found on human beings.

For most of the following descriptions of the flea found on rats in Manila I am indebted to Mr. W. Schultze, assistant entomologist, Biological Laboratory.

Pulex philippinensis, nov. spec., Manila, July 19, 1904. Head, with some very small bristles; front of head high and rounded; eyes round. Above the latter and directed backward are the antennæ, which are club-shaped and consist of three segments. First and third segment equal in size; the third segment cup-shaped; the second segment very small. Superior maxilla elongated, triangular. Palpi maxillarum consist of four segments, of which the last is the longest. The posterior margins of the thoracic segments possess each a row of fine bristles, as do also the abdominal segments. On the latter the bristles extend from the back downward to the middle of the abdomen and from below upward. On the back, on the posterior margin of the eighth abdominal segment are two large bristles. In the male below the external genitals two large bristles on each side—*i. e.*, four in all. Abdomen of the male bent upward. In the interior of its abdomen are the spirally curved internal sexual organs, more or less distinct in different individuals. The abdomen of the female is oval and egg-shaped; on the ninth segment around the external genitals, bristles. In the abdomen of the female between the seventh and the eighth segment is an intestine or sausage-like curved organ, the ovary. Behind it in one individual are several barrel-shaped ova.

The longest bristles are found at the lower ends of the femora. They measure 0.2 mm. in the female, and 0.15 mm. in the male.

Color: Light reddish-brown.

Size of the female: Length, 1.8 mm. to 2.67 mm.; breadth, 0.80 mm. to 1.25 mm.

Size of the male: Length, 1.16 mm. to 1.78 mm.; breadth, 0.70 mm. to 0.75 mm.

Size of the ova: Length, 70 microns; thickness, 55 microns.

Types in the Collection of the Entomological Division of the Biological Laboratory, Bureau of Government Laboratories, Manila, P. I.

Pulex philippinensis appears to be a stationary parasite of the rat. Found in Manila. It is much like *pulex anomalus*, recently described by Baker,[16] and found by him in California. However, the head, eyes, antennæ, palpi, and bristles offer marked points of differentiation.

It is of interest here to mention that Baker, in his monograph on *American Siphonaptera*, describes a new species of rat flea from Brazil, South America. It is a very large species, the male being 3.5 mm. and the female 5.5 mm. in length. Evidently there are quite a few different species of rat fleas in different parts of the world.

Experiments with Flies. Experiments which have been made to demonstrate that plague may be spread by flies are all inconclusive, because the arrangements were such that the transmission of the disease was inevitable. Flies were fed with bouillon containing plague bacilli, and, after varying intervals of time had elapsed, were ground up. The emulsion so obtained was subsequently injected into guinea-pigs or rats, which, of course, died of the disease. Such experiments are inconclusive as far as the possibility of the spreading of plague by flies is concerned.

Experiments were, therefore, so conducted as to imitate more closely what might take place in nature. The organs of plague cases, both from men and from guinea-pigs, were kept in an anatomical glass jar, over which was placed a fly-trap containing a number of flies. The door of the trap was then opened and the flies allowed to come in contact with the plague organs in the lower vessel. After being allowed to remain in the lower vessel for varying periods of time (from one to several hours) they were caused to go up into the trap again by surrounding the lower vessel with some dark material, which made them seek the upper light space. The trap was then closed and placed over an especially constructed fly-proof cage in which had been placed two guinea-pigs. The door of the trap was opened so that the flies could enter the cage. The guinea-pigs had been shaved over an extensive area of the back, and some syrup had been dropped on a few spots, to attract the flies and to cause them to come in contact with the bodies of the animals. This experiment was performed twice, but in neither case did the guinea-pigs contract plague. It had been proved by preliminary trials that the flies which had been allowed to come in contact with and to eat from the organs of plague cases had either in or on their bodies plague bacilli. Flies that had been allowed to come in contact with the plague organs were then caught in a trap, chloroformed, picked up with sterile forceps, and dropped into

slightly alkaline bouillon. In every case the insects gave rise to plague cultures in the media in which they were placed.

Another observation, which was not made experimentally but under perfectly natural conditions, may here be recorded. The San Lazaro Morgue at Manila, a building so constructed as to be insect-proof, owing to the inclemency of the weather, soon got into such a shape that flies could readily go in and out in large numbers. During post-mortem examinations on plague cases flies generally passed freely from the dissected cadavers to those making the examination as well as to others present, and undoubtedly also to persons outside of the building, yet no cases of plague have occurred in the part of the city where the morgue is situated. Hence, no case can be attributed to flies as carriers of the infection.

FIG. 1.

Pulex philippinensis, nov. spec. The flea found on rats in Manila. Male.

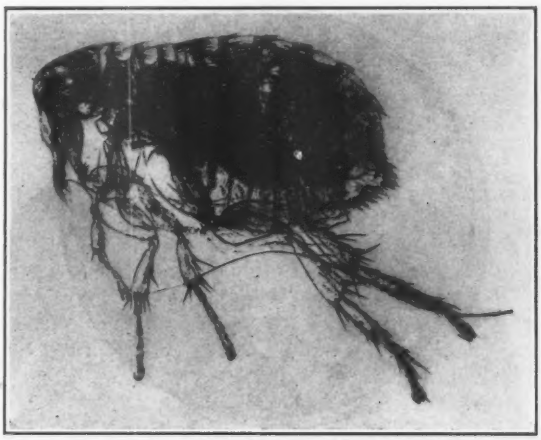
When taking into consideration what has been said above, one is certainly inclined to conclude that insects, as a rule, do probably not play a very important role in the spread of plague. However, that certain parasites may be operative in its transmission is suggested by the observation that this disease is exceedingly prevalent among that caste in Bombay which is probably more infected with pediculi than any other. As stated in the beginning of this paper, a case observed by the writer strongly suggests that pediculi may be carriers of the infection.

A Case of Bubonic Plague in a Child in which the Infection was Possibly Carried by Pediculi. The case in question presented the following findings:

Necropsy No. 910, San Lazaro Morgue, Manila, Saturday, March 5, 1904, 4 P.M. Five hours post-mortem. A girl, aged nine years, residing during life in Anda Street, Intramuros, Manila.

The body of a female child, nine to ten years old, well developed. Post-mortem rigidity strong. Post-mortem lividity well marked and extending over the sides of the body, being particularly noticeable around the neck. The cervical glands on both sides are swollen, imparting a doughy sensation to the touch. The tissues in the neighborhood of the swollen glands are quite œdematous. The integument of the body shows no lesions. There is no discharge from the ears; nor does the external meatus on either side show any ulceration. The mucous membrane of the buccal and nasal cavities

FIG. 2.



The same. Female.

are congested, otherwise normal. The scalp is infected with numerous pediculi, which seem to be ill at ease and run about disturbedly. On section of the body the superficial veins discharge a moderate amount of fluid, very dark blood.

The heart is normal, except that the superficial, subpericardial veins are much injected. The myocardium is somewhat soft, dull, and rather pale, pinkish-yellow in color.

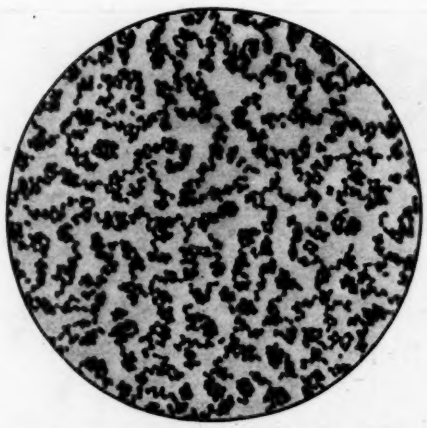
The lungs are pinkish-purple. The lower lobes on the cut surface are dark, reddish-brown, containing much dark, fluid blood, and little air. Some of the areas seen on section are almost in a condition of red hepatization, containing a very large amount of dark, fluid blood. The mucous membranes of the bronchi are slightly swollen, hyperæmic, and moist.

The tracheal mucosa shows the same condition. The larynx is much injected, particularly the epiglottis. The bronchial glands are dark, purplish, slightly swollen, and somewhat softened.

The spleen is of medium size. The capsule is grayish-blue, and smooth as a whole, though slightly wrinkled. The cut surface is reddish-brown. The trabeculæ are well marked. The Malpighian bodies are fairly well visible. The mesenteric glands are reddish-purple, swollen, and rather soft.

Both the kidneys show fairly numerous subcapsular hemorrhagic areas, varying in diameter from about ½ cm. to a mere point. The capsules peel off easily, and after their removal the surfaces show alternating areas, either deeply injected or grayish-yellow. On

FIG. 3.



Cover-glass preparation of twenty-four-hour-old agar culture of the plague bacillus derived from pediculi. Oil-immersion magnification.

section the vessels appear highly congested, and the glomeruli stand out as deep, reddish-gray points. The tubules are grayish-yellow; the pyramids are deeply injected. The mucous membrane of the pelves is smooth and slightly swollen, but not hemorrhagic. The substance of the kidneys is soft and almost gelatinous. The suprarenals are large, swollen, congested, and very soft.

The surface of the liver is bluish-pink, mottled with pale, grayish-yellow areas. The capsule is smooth. The cut surface is grayish, pinkish-yellow. The veins contain a good deal of dark, fluid blood. The gall-bladder contains a turbid, yellowish bile; its mucous membrane is smooth.

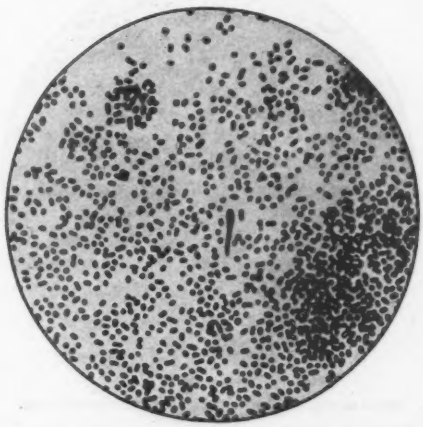
The serosa of the stomach and intestines is injected. The superficial veins are marked as reddish lines. The mucosa, as a whole,

is moderately injected, with punctiform hemorrhages in the ventricular mucosa. The intestinal lymph follicles are somewhat swollen. The peritoneal covering of the uterus and tubes is much injected. All of the fine superficial vessels are visible in consequence of the marked congestion.

The cervical glands on both sides, including those along the sternocleidomastoids and the deeper submental ones, are enlarged, highly congested, and softened. On section a good deal of dark, bloody juice can be scraped from the surface. The smears made from the gland juice show numerous typical plague bacilli.

Anatomical Diagnosis. Hemorrhagic, acute, parenchymatous nephritis. Congestion and œdema of the lungs. Moderate fatty degeneration of the liver. Hemorrhagic inflammation. Hypertrophy and softening of the cervical glands on both sides. A more or less general hypertrophy of most of the lymph glands. Bubonic plague.

FIG. 4.



Cover-glass preparation of a sixteen-days-old glycerin-agar culture of plague bacilli. Involution forms Magnification same as above.

Pieces from the liver, both kidneys, and the cervical glands were placed in Zenker's fluid during the post-mortem examination.

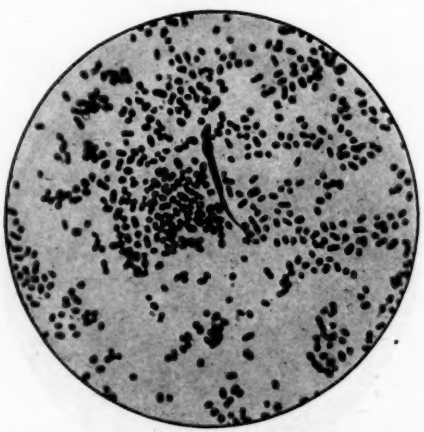
Before the body had been opened three pediculi were picked from the scalp with sterile forceps and dropped into empty sterile test-tubes and later into three flasks, each containing 50 c.c. of sterile, slightly alkaline bouillon. All of the three flasks developed cultures of plague bacilli. The cultures were then transferred to various media, and the bacteria were fully identified as typical plague bacilli. One culture from the spleen and two from the cervical glands likewise developed plague bacilli.

Since this child, dead from bubonic plague, had come from a district which had been considered plague-free for some time, inquiries were made as to the possibility of the girl having been infected with pediculi from some one living in an infected district.

Dr. R. E. S. Newberne, District Medical Inspector, reported on the matter as follows:

"So far as the records show only two cases of bubonic plague, prior to the one under discussion, have occurred on Calle Anda, the first in 1900 at No. 11, and the second in 1901 at No. 137. These numbers being a considerable distance from No. 89 and in opposite directions, it may be assumed that the district is not infected.

FIG. 5.



Same as Fig. 4. Spermatozoa-like involution forms.

"The orphan was taken to 89 Anda Street from the Hospicio de San Juan, December 24, 1903, and remained in good health until the last days of February, when she became ill, complaining of earache and fever, which did not yield to local treatment. The patient was sent to San Juan de Dios Hospital about March 4th, where she died twenty-four hours later, after an illness of nine days.

"So far as can be ascertained, this child did not handle rats or do anything else to which the infection could be ascribed. She slept on a petate on the floor of one of the upstairs rooms, as is the custom of Filipino children.

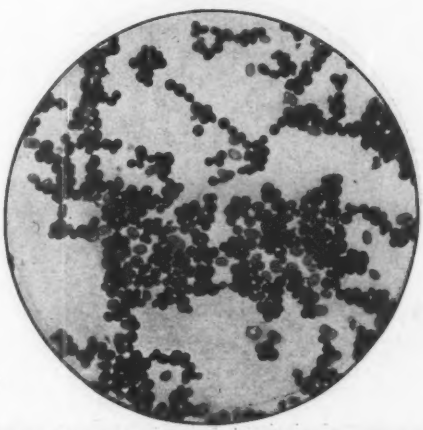
"With the exception of the time—from February 7th to 16th—when she attended the public school, she did not associate with children outside of her home. The family assert that she was free from vermin when she was sent to the hospital, though it was admitted that Filipino children are generally infected with *ped-*

iculi capitis. Five bed-bugs, found in the crack of the floor upon which she slept, have been sent to the laboratory; also thirteen rats were sent."

Mr. Charles B. Hare, assistant bacteriologist in the Biological Laboratory, who examined the rats, did not find any evidence of plague in them. Smears were made from the five crushed bed-bugs, which likewise did not show any plague bacilli. It was intended to test the bed-bugs by cultural methods, but this was overlooked by mistake.

Histopathology of the Case. Pieces of tissue from the primary cervical bubo, from both the kidneys and from the liver, were fixed in Zenker's solutions, sectioned and stained by various methods, including Weigert's fibrin stain.

FIG. 6.



Cover-glass-preparation of a three-days-old 4 per cent. salt-agar culture of plague bacilli, showing the yeast-like involution forms. Magnification same as above.

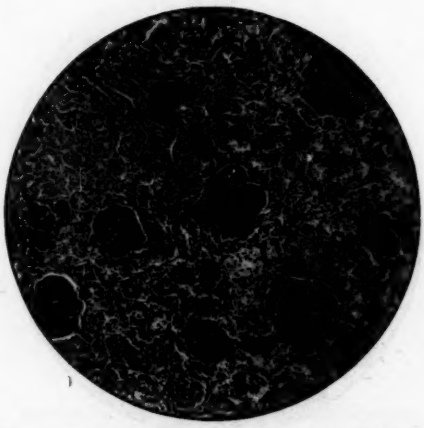
Sections from the cervical glands show, even on superficial examination, a number of most profound changes, namely: 1. Almost complete loss of the normal structure and differentiation of the gland into cortical follicles and medullary cords. 2. Advanced coagulation necrosis. 3. Extensive free-blood extravasation. 4. Deposit of granular and fibrillar fibrin. 5. The presence of enormous solid, irregularly distributed masses of bacteria.

The deeper portions of the cortex still present some oval compartments outlined by fibrous connective tissue, evidently once the trabeculæ; the latter, however, do not surround any normal lymph follicles, but masses of necrotic tissue and free extravasated blood. Where the dense masses of bacilli are located there are few tissue elements left. The cells which are still recognizable as such are

mononuclears, and their nuclei generally show a marked pyknotic condition. At the margin of the bacillar masses and clumps there are more normal mononuclear and polynuclear cells, among which are quite a few eosinophiles. Almost as numerous as the latter are plasma mast cells. Bacilli are found also in the tissue next to the large colonies. The bacilli here do not form solid, dense masses, but are freely distributed among the cells. Intimately mixed with the leukocytic cells and the bacilli are numerous red blood corpuscles.

The peripheral tissue, next to the capsule, show a dense infiltration, with completely degenerated erythrocytes and with hæmatoidin and hæmosiderin. This zone apparently is part of the former lymph sinus, which, however, can no longer be distinctly recognized as such. Here, likewise, numerous bacilli are found.

FIG. 7.



Section of kidney in a case of bubonic plague. Stained with Weigert's fibrin stain and showing hyaline thrombi in the glomerular vessels. Zeiss AA Comp. Oc. No. 4.

Fibrin is quite irregularly and extensively distributed throughout the gland. In its interior it is found to be in the form of a granular deposit, and also in the shape of coarser or finer threads. Around the dense masses of bacilli it occurs in the form of a fibrillar network, sending fine threads into masses of micro-organisms.

The tissue next to the capsule—*i. e.*, the former lymph sinus—likewise contains a network of fibrin. The small vessels are more or less completely occluded by hyaline (fibrin) thrombi. These are seen both in the interior of the gland and in the capsular vessels. Here and there the fibrin extends from the interior of a vessel, through its wall into the perivascular tissue.

Few bacilli or none at all are found in the bloodvessels, both in those with open lumina as well as in those where the latter are

occluded by a hyaline thrombus. This condition prevails even in vessels surrounded by innumerable bacilli. The picture clearly furnishes histological evidence that bubonic plague is not primarily a hæmatogenous infection, and that, while the lymphatic infection may be enormous, the blood may still be little invaded by *bacillus pestis*.

The bacteria found so numerously in the sections of the glands show all the morphological characteristics of plague bacilli.

Kidneys. The renal tissue presents a most striking picture. Sections from both kidneys, treated by Weigert's fibrin method, look as if the vessels had been injected with a violet-stained gelatin. There is not a normal glomerulus seen anywhere. All the sections show a more or less complete obliteration by hyaline thrombi. In

FIG. 8.

most of the Malpighian bodies the hyaline thrombosis of the capillaries is so perfect that both the main branches of the afferent vessel and the smaller capillaries given off from the larger loops are sharply outlined.

Most of the thrombi appear to be perfectly solid; some, however, exhibit a hollow space in the centre, as can be seen both in transverse and in longitudinal sections.

The endothelial lining of the thrombosed vessels is well preserved. Where the thrombi are comparatively thin one can see, both in longitudinal and in transverse sections, endothelia which are perfectly normal to all intents and purposes. Nowhere do the thrombosed vessels show to any extent a loss of endothelia. The thrombosis can, therefore, not be attributed to a denudation of the vessels of their endothelial lining. L. Loeb[17] a short time ago reported

some experiments on certain conditions of blood coagulation. He concluded that after the removal of the endothelial lining specific enzymes are extracted from the tissues and so act upon the fibrinogen, which is held in colloidal solution, that fibrin is precipitated. Since in our case a loss of endothelia in the thrombosed vessel is not demonstrable, the thrombosis cannot be attributed to such a loss. Perhaps the hypothesis that toxic influences may have so damaged the endothelia that they became permeable to the substances producing coagulation, is justifiable. Such disturbances of the functions of cells by toxic influences without demonstrable morphological changes are, of course, not unknown.

FIG. 9.

The capsules of Bowman are likewise normal, though a few of them show a very moderate amount of thickening; their lining epithelium exhibits no marked changes. In some places the hyaline thrombi are continued into the vasa afferentia and efferentia and even into the vessels of which these are branches. Quite commonly there are seen between the uriniferous tubules parts of such small vessels filled with hyaline thrombi. However, none are found in the larger arteries or veins, in some of which finely granular fibrin and desquamated endothelial cells are present. The vessel walls themselves show no damage aside from the denudation of the intima. There is in particular no extension of the fibrin through the vessel walls, nor is there any evidence of mesophlebitic or periphlebitic or arteritic processes.

The epithelial cells lining the convoluted uriniferous tubules are somewhat swollen, with indistinct outlines and a vacuolated protoplasm, but their nuclei are yet quite normal. A granular material

partly fills some of the convoluted tubules. The epithelial lining of the straight tubules does not show any marked changes. The capsule of the kidney is normal. Nowhere do any of the renal bloodvessels show a large number of plague bacilli, a few of which are possibly seen inside the lumina of bloodvessels; but even this is not certain, being, on the contrary, rather doubtful. A moderate number of bacilli, however, are seen in the lymph clefts between the tubules and around the Malpighian bodies.

The profound vascular change, the complete obliteration of capillaries, small veins and arteries by a homogeneous, hyaline material is apparently due to toxic influences.

A few slender, long bacilli, which keep Gram's stain, are occasionally found in the tubules. They are probably of no significance and represent an agonal or post-mortem invasion.

FIG. 10.

Section of kidney in a case of bubonic plague. Stained with Weigert's fibrin stain and showing hyaline thrombi in glomerular vessels. Oil-immersion magnification.

Welch[18] has reported an observation of complete glomerular, capillary, hyaline thrombosis which is identical with the one described above. In his article on "Thrombosis," in Allbutt's *System of Medicine*, he says: "The most striking example of this form of (hyaline) thrombosis with which I am acquainted is encountered in the renal capillaries, chiefly of the glomeruli, of swine dead of hog-cholera, or of animals infected with the hog-cholera bacillus. In extreme cases there is complete anæmia, and it may be impossible to force more than a minimal amount of injecting fluid into the renal vessels. Sections stained with Weigert's fibrin stain look as if the capillaries had been injected with Berlin blue. Ribbert found similar hyaline thrombi in the kidneys of rabbits inoculated with

staphylococcus pyogenes aureus. I have repeatedly found them in various experimental infections and in human infections. They occur in eclampsia. Bacteria are not necessarily present, so that toxins are probably the underlying causative factor, and for this there is experimental evidence."

Hyaline thrombosis of the glomeruli vessels is not a rare occurrence in plague, because we have encountered it seven times in the study of about twenty cases of this disease.

Sections of the liver show a very few small periphlebitic inflammatory foci composed of small, round mononuclears. The liver cells all show a coarse vacuolation, some of the vacuoles being larger than the nuclei. The capillaries are moderately filled. There is no free, extravasated blood. A very few plague bacilli are found between the liver cells.

A study of this case shows it to be one of bubonic plague, with the cervical glands as the seat of the primary bubo. In the absence of all wounds on the head, the neck, the mucosa of the nose, the buccal cavity, etc., and in view of the fact that plague bacilli could be demonstrated in the pediculi, it is perhaps not unreasonable to consider it probable that in this case the infection was conveyed through the bite of pediculi coming from another individual infected with plague.

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REVIEWS.

LECTURES TO GENERAL PRACTITIONERS ON THE DISEASES OF THE STOMACH AND INTESTINES. By BOARDMAN REED, M.D. New York: E. B. Treat & Co., 1904.

THE literature of diseases of the stomach and intestines is constantly being enriched to keep pace with recent advances in methods of diagnosis and treatment, and this, the most recent American contribution in the form of a course of lectures delivered by the author to his students, is intended to present "in a single volume the whole subject of diseases of the stomach and intestines from the standpoint of our present knowledge," without professing to enter into profound discussions of the many questions that are still *sub judice*. The lecture style which the author has chosen is more in keeping with direct, at times, perhaps, dogmatic statement, than with academic discussion; yet, although his teaching represents mainly his own views, his attitude is that of a conservative physician, a careful student of other men's ideas and experience in a subject in which a wide divergence of opinion obtains on questions of vital importance to the life and welfare of patients.

In the physical examination of the abdomen the writer recommends the simpler clinical methods which can be carried out without complicated apparatus and without causing the patient discomfort; in ordinary cases he relies chiefly on percussion and the effect of filling the stomach with water (clapotement) to determine position and size, as well as motility of the stomach. Inflation with carbon dioxide, he, in agreement with most other authorities, regards as a useful and perfectly safe procedure, but uses hydrochloric instead of tartaric acid, with bicarbonate of soda to produce the carbon dioxide. The lectures on uranalysis and examination of the feces and blood at least do not err on the side of prolixity; but the part devoted to the feces is disappointing. Writers on gastric and intestinal diseases are fond of dwelling on this subject of the examination of feces and of deploring the lack of interest on the part of the general practitioner; but aside from pathogenic bacteria and possibly the ova of parasites, the findings obtained with the microscope add but little to the information obtained by naked-eye examination, which no careful diagnostician would think of neglecting.

The last lecture in the section devoted to diagnosis is entitled a "Symptomatic Guide to Diagnosis," and contains a list of symptoms, arranged in alphabetical order, with a list of possible causes

in a parallel column opposite. Now, this method of approaching the difficult subject of diagnosis, which imitates the actual conditions that confront the doctor when he sees the patient for the first time, has been successfully employed by certain authors, notably in England, and might with advantage to the student be exploited more generally by systematic writers. But the author has, unfortunately, contented himself with the mere enumeration of individual symptoms on the one hand and etiological factors on the other, which is really no guide at all, as it does not afford the slightest hint to help the bewildered student in arriving at anything like a definite conclusion in a given case. If, instead of individual symptoms, the author had presented a series of clinical syndromes, and if, instead of attempting to give every conceivable etiological factor, he had contented himself with the most probable causal condition, the practical value of this chapter would have been very much greater.

Of the 178 pages devoted to methods of treatment (Part III.), 140 are taken up with methods other than drug-giving, and the remaining 38 with the medicinal therapy of the diseases of the stomach and intestine. A large portion of this space is devoted to dietetics and contains a sufficiency of tabular matter showing food values, the requirements of different classes of individuals, the ingredients contained in different food articles, and the author's progressive series of diets, besides Leube's and Penzoldt's diet schemes, with some sound criticisms of the latter from the American point of view.

As the armamentarium of a specialist in diseases of the stomach is not complete without electrotherapeutic apparatus, so an up-to-date text-book would not be complete without a full description of the various forms of electricity that are now used in the treatment of patients. Among the newest of these methods are the high-frequency and so-called polyphase electric currents. The high-frequency currents, we learn, are most suitable for application within cavities from the fact that they produce practically no sensation. Other special methods, such as Cleaves' hydroelectric treatment within the bowel and the like, are also mentioned, but without critical comment. Whatever kind of electricity is employed, it appears that the effect, with one exception, is constantly the same—in one word, *tonic*—and the conditions that are benefited by electric treatment are, therefore, gastric dilatation, atonic dyspepsia, and, in fact, all atonic conditions. The interesting exception, according to the author, is that with a high-tension coil, which, being practically painless, permits the application of a strong current, the function of the gastric glands can be depressed; that is, hyperchlorhydria is diminished. The author makes extensive use of the intragastric faradic current, for which he has designed an electrode modified from Einhorn. He contends that the procedure is as easy of application as lavage.

Hydrochloric acid stimulates the secretion of the gastric glands and does not inhibit fermentation; it should be combined with pepsin, as a rule, and a smaller dose than that advised by most authorities is recommended: from 4 to 5 drops of the dilute acid after meals up to 10 drops, and, in exceptional cases, 20 or 30 drops in a tumblerful of water, which he patient is directed to sip slowly. His experience must have been rather exceptional on this point, and he appears to regard the drug purely as a stimulant to secretion.

Alkalies in small doses stimulate and in large doses diminish the production of hydrochloric acid, irrespective of the relation between administration and the ingestion of food. The truth about this much-debated question probably is that when the stomach is full and a large portion of the acid has already combined with the food, a smaller dose of the alkali suffices to neutralize the remaining excess of hydrochloric acid; in short, the dose must be adapted to the quantity of acid to be neutralized at the time of administration. With papoid, caroid, and other digestants of the same class, the author's experience appears to have been as disappointing as that of most physicians who have given these substances a thorough trial.

The lecture on the treatment of appendicitis contains a critical review of the different schools, of which there are three, according to our author. The radical surgical school, represented by Deaver, of Philadelphia; Morris, of New York, and Murphy, of Chicago; the conservative school, comprising a large number of prominent surgeons, Keene, Richardson, White, Parke, and a long list of others; and the "surgico-starvation method," advocated by Ochsner. While the author's attitude is impartial and his judgment is based on the results reported by exponents of each of the three methods, it is not difficult to see that he is, if not entirely convinced, at least very strongly impressed by the teaching of Ochsner.

A succinct epitome of the surgery of the stomach and intestines completes the volume, which, considering the generous size of the type and illustrations, has been kept within reasonable limits, while a very good working index makes up for the somewhat unwieldy length of the table of contents. R. M. G.

SERUMS, VACCINES, AND TOXINS IN TREATMENT AND DIAGNOSIS. By WILLIAM CECIL BOSANQUET, M.A., M.D. Oxon., F.R.C.P. London. Chicago: W. T. Keener & Co. London: Cassell & Co., Limited, 1904.

DR. BOSANQUET in this small book has collected much information which is both useful and interesting. Instead of an enthusiastic, unscientific plea for the use of these newer remedies, one finds a just treatment of facts in which statistics are given and original author-

ities are quoted. The opening chapters present a short *résumé* of the modern conceptions of immunity developed particularly along the lines of the "side chain" theory of Ehrlich. Then come chapters upon the preparation and administration of serums and vaccines, and the use of serums and toxins in the diagnosis of disease. The major portion of the book, however, deals with the treatment and prevention of various diseases by means of antisera, antitoxins, and vaccines. To all the important affections a separate chapter is devoted. The book is essentially modern, but on account of the very fact that it deals with problems which are in the process of building, its greatest value and interest are for the present alone.

W. T. L.

ESSENTIALS OF MEDICAL CHEMISTRY, ORGANIC AND INORGANIC, CONTAINING ALSO QUESTIONS OF MEDICAL PHYSICS, CHEMICAL PHILOSOPHY, ANALYTICAL PROCESSES, TOXICOLOGY, ETC. Prepared especially for students of medicine. By LAWRENCE WOLFF, M.D. Sixth edition, thoroughly revised, by A. FERREE WITMER, PH.G. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

SINCE this small book has gone through six editions, there must be a demand for it, though a study of even this last revised edition fails to explain the reason. In the mass of questions and short answers new material may be found here and there. The term "Chemical Philosophy" seems to appear only in the title. The book represents the typical "Quiz Compend."

W. T. L.

SURGICAL EMERGENCIES: THE SURGERY OF THE ABDOMEN. Part I. Appendicitis and Other Diseases about the Appendix. By BAYARD HOLMES, B.S., M.D., Professor of Surgery in the University of Illinois; Professor of Clinical Surgery in the American Medical Missionary College, Chicago; Attending Surgeon to the Chicago Baptist Hospital. New York: D. Appleton & Co., 1904.

THIS small volume contains a large amount of material. It represents the author's experience in the treatment of appendicitis and some other abdominal diseases, and a careful consideration of the pathology and symptoms of each. One is impressed with the author's earnestness and conviction regarding his views, but at the same time he is open to the criticism of being anything but generous respecting the views of others. A large part of each chapter is taken up with minute reports of cases. His criticism of the Ochsner treatment is unnecessarily severe; he does not, however, attach Ochsner's

name to the treatment. He classifies it with osteopathy and Christian Science. Although we agree with the author that every case of appendicitis should be operated upon, and that medical treatment should be given no place excepting when operation is impossible, we regret the light way in which he speaks of the opinion of recognized authorities. He also shows a tendency to illustrate his remarks by a discussion of his own successes and others' failures. His after-treatment probably shows his individuality more than anything in the book. After a simple removal of the appendix the patient is allowed to walk to his room from the operating-table if a local anæsthetic has been used; to get out of bed on a commode, or sometimes to go to the closet for the purpose of urination or defecation; to sit up in his chair at his meals on the day following operation, and after that is allowed to walk about the hospital. A list of twenty-nine cases operated upon during twelve months is given, in which the time spent in bed varied from five hours to twenty-one days. Thirteen of these patients were out of bed in forty-eight hours or less. The administration of liquid and semiliquid diet in the simple cases is begun within a few hours after the operation. No abdominal support is advised, and no restriction as regards exercise is made. It is stated that the patient should be able to leave the hospital within a week.

The closing portions of the book deal with peritonitis, some of the varieties of intestinal obstruction, perforated typhoid ulcer, and malignant disease of the intestine. The book closes with several pages of adages. The reader is impressed at once with the author's clearness of statement, his absolute conviction in the various positions taken, and especially those in which he differs from a large majority of surgeons. J. H. G.

THE SURGERY OF THE HEART AND LUNGS. A History and Résumé of Surgical Conditions found therein, and Experimental and Clinical Research in Man and Lower Animals, with reference to Pneumonotomy, Pneumonectomy, and Bronchotomy, and Cardiotomy and Cardiorraphy. By BENJAMIN MERRILL RICKETTS, Ph.B., M.D., Member of the American Medical Association, Western Surgical and Gynecological Association, International Medical Congress, 1887, etc. New York: The Grafton Press, 1904.

THE advancement which has been made during the past few years in the surgery of the heart is simply remarkable. The medical journals have been full of reports of interesting and unusual cases, especially of stab wounds treated by surgical operation. The subject is one of peculiar interest to all surgeons, and there is naturally a demand for a book devoted to this subject.

The author has contributed largely to the surgery of the heart and lungs, especially the experimental side of the subject, and with his papers many are no doubt familiar. A large part of this book is devoted to history and bibliography, and is consequently made up largely of quotations and references. This portion, therefore, will be found of inestimable value to anyone who wishes to look up the surgery of either the heart or lungs. No attempt has been made on the author's part to consider all the diseases of the heart and lungs, but only those which may require surgical interference. He has been most careful to verify all his statements with references. The original part of the work consists in a report of his extensive experimental work on dogs.

This book is a most valuable contribution, and one for which we bespeak a marked success. J. H. G.

A Text-book of Clinical Diagnosis by Laboratory Methods. For the Use of Students, Practitioners, and Laboratory Workers. By L. Napoleon Boston, A.M., M.D., Associate in Medicine and Director of the Clinical Laboratories, Medico-Chirurgical College, Philadelphia; formerly Bacteriologist at the Philadelphia Hospital and at the Ayer Clinical Laboratory of the Pennsylvania Hospital. With 320 illustrations, many of them in colors. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

Beginning with an explanation of the mechanics of the microscope itself, the author has taken pains to be explicit in his account of the various techniques. The opening chapter considers the care and use of the microscope and its accessories, and explains the laws of refraction and the values of the different lenses usually employed. This attention to detail is manifest throughout the book.

In the section on blood there is a complete description of its examination in health and disease, including a study of cryoscopy and osmosis. Later, the different diseases of the blood are taken up, and their special pathology and bacteriology studied seriatim. The author has, unfortunately, not been so systematic in the chapters devoted to the analysis of urine, but has, however, given an exhaustive treatise on that subject.

A very good account of animal parasites is included under the different chapters on the blood, the urine, and feces. The examination of the secretions of the nose, eye, mouth, and the genital organs is taken up in the latter part of the book, as is also the analysis of milk and the study of the parasitic skin diseases.

There are over 300 illustrations, with a number of colored plates, those illustrative of the malarial parasite being especially noteworthy.

With perhaps the exception of the section on the urine, the contents of the volume are remarkably well arranged, and the work will be of considerable value to those to whom the ready access to a modern clinical laboratory is not practical. A. N.

A TEXT-BOOK OF HUMAN PHYSIOLOGY. By ALBERT P. BRUBAKER, A.M., M.D., Professor of Physiology and Hygiene in the Jefferson Medical College; Professor of Physiology in the Pennsylvania College of Dental Surgery, etc. With colored plates and 354 illustrations. Philadelphia: P. Plakiston's Son & Co., 1904.

INASMUCH as this book is written for the medical student and practitioner, and is designed particularly to present the more important facts of physiology which have to do with the practical aspect of medicine, much of the technical portion of the subject is omitted, and the normal functions of the various organs and systems are related in an interesting and readable manner. The treatment of the subject is developed along the usual lines, and does not differ especially from other text-books of this nature. The paragraphing is well arranged, so that one can readily refer to any particular subject. One might mention a few instances, as in the discussion upon the origin of leukocytes, or upon the histology of the lymphatics, where the author's statements do not coincide with the current views concerning these subjects, but with a few exceptions the book is generally good. W. T. L.

A TEXT-BOOK OF PATHOLOGY. FOR PRACTITIONERS AND STUDENTS. By JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia; Pathologist to the Philadelphia Hospital, and to the Medico-Chirurgical Hospital, Philadelphia. With 350 illustrations, a number in colors. Philadelphia, New York, and London: W. B. Saunders, & Co., 1904.

THIS work of 818 pages is a systematic treatise on general and special pathology. The ground, as far as the principles of pathology are concerned, is well covered, and the arrangement of the book is good. The subject of general pathology is first discussed. Here the questions of general etiology, defects of development, pathology of nutrition and of the circulation, characteristics of cell life, retrogressive and progressive tissue changes, parasitism, immunity, and infection are taken up. The accepted teachings are usually set down, but the "pros and cons" of the various undecided points are not, as a rule, given.

Under the heading of Special Pathology, the diseases of the various systems and organs are taken up in a well-ordered manner, the degenerations, hypertrophies, infections, etc., of each being discussed. A voluminous index of fifty-four pages adds to the value of the book. The size of the book is, perhaps, a fault, as it contains more than is really needed in teaching the subject to students of medicine, while it hardly covers the field of pathology with enough comprehensiveness to satisfy one as a work of reference.

The author's style is somewhat elaborate in places, and clear conceptions are not at all times given. The book contains some good photographs, while the drawings are of average quality. It presents an attractive appearance. G. C. R.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Comprising ten volumes on the Year's Progress in Medicine and Surgery, issued monthly. Under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-graduate Medical School. Vol. IX. Physiology, Pathology, Bacteriology, Anatomy. Dictionary edited by W. A. EVANS, M.S., M.D.; ADOLPH GERHMANN, M.D., and WILLIAM HEALEY, A.B., M.D. Chicago: The Year Book Publishers, 1904.

THIS number preserves the same general form and arrangement as the preceding ones. The reviews are, as usual, quite full and comprehensive, while much of the important work of the year, particularly that possessing practical interest, is touched upon. The majority of the references, however, are confined to English and American authors.

It is very unfortunate that, evidently in binding, a portion of the authors' index should have been omitted. W. T. L.

A TEXT-BOOK OF PHYSIOLOGICAL CHEMISTRY. FOR STUDENTS OF MEDICINE AND PHYSICIANS. By CHARLES E. SIMON, M.D. Second edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS second and enlarged edition of Dr. Simon's book should be particularly appreciated just at this time, for of late the extensive and important researches in physiological chemistry have rendered much service to medicine in general. Use has been made of these recent contributions and there is evidence of much revision. Particularly noteworthy are the chapters on Albumins, on the Products of Nitrogenous Katabolism, and on Gastric and Tryptic Digestion. Though the book is "intended as a text-book for the lecture-room

and as a guide in the physiological-chemical laboratory," many of the chapters may be read with great interest away from the laboratory. At the same time there is an appendix of laboratory exercises which serves as a guide to the student in performing certain experiments. The book should prove to be very useful. W. T. L.

A PRACTICAL TREATISE ON DISEASES OF THE SKIN. FOR THE USE OF STUDENTS AND PRACTITIONERS. By JAMES NEVINS HYDE, A.M., M.D., Professor of Skin, Genito-urinary, and Venereal Diseases, Rush Medical College, Chicago, etc., and FRANK HUGH MONTGOMERY, M.D., Associate Professor of Skin, Genito-urinary, and Venereal Diseases, Rush Medical College, Chicago, etc. Seventh and revised edition, illustrated with 107 engravings and 34 plates in color and monochrome. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS well-known treatise upon diseases of the skin has again been subjected to an extensive and thorough revision by its authors. In addition to a considerable number of new sections descriptive of diseases not considered in previous editions, much new material has been added to the old sections, many of which have been entirely or in large part rewritten. So far as we have observed, nothing of any real importance among the recent acquisitions to our knowledge of diseases of the skin has been overlooked.

Among the most interesting and important of the new sections introduced are those devoted to the consideration of radiotherapy and phototherapy. The *x*-ray and light bid fair to take rank among the most important additions for many years to the armamentarium of the dermatologist, and the indications for the employment of these powerful agents in diseases of the skin and the method of using them are treated in a manner commensurate with the importance of the subject.

Under the title "Psoriasiform Dermatoses," a group of affections is described whose members have been reported in the past fifteen years under a great variety of names by different observers. Brocq, who has recently written at some length upon this group, has proposed to name it *parapsoriasis;* as this seems to us a fairly unobjectionable designation, we think the authors, instead of adding to the huge burden of names under which dermatology has so long groaned, might well have adopted it.

We note that the section which in former editions appeared under the title "Dermatoses of Scrofulous Subjects" is now called "Dermatoses Probably Tubercular," an unmistakable indication of the marked change which has taken place in the manner of viewing this most important group of diseases.

The value of the book has been much enhanced for workers in

this branch of medicine by the great increase in the number of references to the literature of dermatology.

This new edition will easily take rank among the three or four best books upon cutaneous diseases. It is a clear and comprehensive exposition of the most modern views upon the subject, and we heartily recommend it to those who wish to have the latest word upon diseases of the skin. M. B. H.

THE STUDENT'S HANDBOOK OF SURGICAL OPERATIONS. By SIR FREDERICK TREVES, Bart., K.C.V.O., C.B., LL.D., F.R.C.S., Sergeant Surgeon-in-Ordinary to H. M. the King; Surgeon-in-Ordinary to H. R. H. the Prince of Wales; Consulting Surgeon to the London Hospital. New edition, revised by the author and JONATHAN HUTCHINSON, Jun., F.R.C.S., Surgeon to the London Hospital; Examiner in Surgery, Royal Army Medical Department. (Abridged from the author's *Manual of Operative Surgery.*) Chicago: W. T. Keener & Co., 1904.

THE present volume is a condensation of the author's more extensive work, which is so well known to the profession. For a book of its size it contains a wonderful amount of information and is excellently illustrated. It can be heartily commended for the use of students. The arrangement is the same as in the larger work, and the most essential features of the various operations are emphasized. It differs from the larger work in that the general principles of operative surgery and a consideration of the value of the various methods are not discussed. The anatomy of the various parts, the treatment after operations, the mortality, and the results are also omitted.

J. H. G.

THE UTERO-OVARIAN ARTERY, OR THE GENITAL VASCULAR CIRCLE. Anatomy and Physiology, with Their Application in Diagnosis and Surgical Intervention. By BYRON ROBINSON, B.S., M.D. Chicago: E. H. Colegrove, 1903.

THE description given by the author of the utero-ovarian artery, or, as he calls it, the genital vascular circle, is very complete. The illustrations are very numerous, but many of them might be omitted, because of their great similarity to others. It is evident that the author has expended a great deal of time and effort in the preparation of this work. J. H. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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AND

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The Significance of Pulmonary Infusions in the Diagnosis and Therapy of Pulmonary Tuberculosis.—P. JACOBS (*Deut. med. Woch.*, 1904, xxx. 945) says that on guinea-pigs he was able to show that large quantities (5 to 15 c.c.) of fluid could be injected directly into the lung through a catheter passed into the large bronchi without producing any apparent distress to the animals and without being followed by any untoward symptoms. By using various substances (aniline blue, salicylic acid) it was demonstrated that the fluid was thoroughly distributed throughout the lung, that the substances were well borne, and that they were retained for a relatively long time in the pulmonary tissue. If drugs can exert any local effect upon tuberculous processes this direct method of application offers many evident advantages over their administration by mouth or subcutaneously. Together with Bougart the process was tried upon tuberculous cattle, various substances being employed. The five cows used in the experiment received repeated injections of 500 c.c. of fluid during the six months of observation, an average of twenty-five injections per cow, always stood the operation well, and showed no ill effects from the numerous infusions. The fluid was introduced through a soft rubber catheter passed through a tracheotomy tube. The medicaments used were hetol, creosote, tuberculin, methylene blue, and pyoktanin. As a general result, it may be stated that the four cows killed at the end of six months showed improvement, two of them even marked improvement; but in the one treated with pyoktanin the course of the disease was uninfluenced and the animal succumbed. Tuberculin was found to be the most efficacious remedy, then creosote, hetol, and methylene blue in the order named. Anatomically the lungs from the cows treated with tuberculin and creosote showed a definite process tending toward arrest and healing. Together with Dr. Rosenburg the method was then tried on human patients, a soft rubber catheter being passed into the trachea through the larynx. The technical difficulties were soon overcome, and the infusions, as in animals, were well borne. Five cases were treated,

and Jacobs feels justified in concluding that the method is harmless and the therapeutic results encouraging. As an important accessory contribution, he believes the infusion is of great value as a diagnostic procedure. In the presence of pulmonary tuberculosis the patients react to one-tenth or one-twelfth of the dose of tuberculin necessary for a rise of temperature by subcutaneous injection, whereas if the tuberculous lesion be elsewhere in the body it requires the same or even a higher dose by infusion than by subcutaneous injection.

Arteriosclerotic Abdominal Pain.—MAX BUCH (*St. Petersburger Med. Wchnschr.*, 1904, vol. 29, No. 27, p. 298). On the basis of an analysis of 25 cases—collected from the literature and from his own observations—Buch draws a clinical picture which he considers distinctive of sclerosis of the vessels in the splanchnic area. The significance of this symptom-complex is an acquisition of the past few years and is a valuable addition to our knowledge of the manifestations of arteriosclerosis in other regions of the body, the sclerosed coronary arteries, arch of the aorta, cerebral, renal, and femoral vessels giving rise to definite and easily appreciated features. The essential mark of all the cases is abdominal pain, but on account of certain secondary features he divides them into two classes. In the first class the abdominal symptoms dominate the picture. The patients, usually over forty years of age, are seized with severe attacks of abdominal pain lasting from a few minutes to an hour and situated almost always above the navel. The attacks recur frequently, often many times a day, and are precipitated by the same factors which are of such importance in the occurrence of paroxysms of angina pectoris, bodily exertion, emotional disturbances, and assuming the horizontal position. In some of the cases attacks of stenocardia occur between the attacks of abdominal pain. In most of the cases there are the evident signs of arteriosclerosis in other regions. The abdominal aorta is seldom enlarged or misplaced, but is constantly tender, the sensitiveness being more marked during the paroxysms. In the experience of Buch all the cases yield rapidly to diuretin or strophanthin, and he sees in this a valuable therapeutic means to test a doubtful diagnosis.

In the second class of cases the epigastralgia is associated with true angina pectoris or anginoid attacks. This group of cases has long been recognized and is well described by Huchard and V. Schrötter. The epigastric pain may initiate the attack or be referred to merely as a radiation of the thoracic pain.

As a rule there are no digestive disturbances in any of the cases and the ingestion of food bears no other relation to the attacks than that too full a meal may precipitate them. Only exceptionally is there meteorism. It must be remarked that there may be, as in other parts of the body, extensive sclerosis of the abdominal vessels without any symptoms. Buch reviews at length the probable causes of the pain.

A Contribution to the Study of Hemorrhage from Apparently Normal Kidneys.—HUGO SCHÜLLER (*Wiener klin Wochenschr.*, 1904, xvii. p. 477) reports a case of unaccountable renal hemorrhage in a woman, aged forty-nine years. The onset occurred during a menstrual period, and was associated with fever, vomiting, and headache, which lasted for a day. The hemorrhage, which at first lasted for three months,

was at one time so extensive as to produce marked anæmia, which confined the patient to bed for a month. Six months after onset the right kidney, from which the blood was found to come, was opened on operation by the usual autopsy incision. No gross lesions were found. An examination of a bit of excised kidney showed, however, evidence of an old inflammatory process—*i. e.*, "the presence of small cysts, some containing a colloid material. Occasionally a hyaline cast is found in the straight tubules, but they are more numerous in sections from the regions of the pyramids. The casts stain so deeply and the epithelial cells about them appear so flattened that one may conclude they have been lodged there a long while. In places red blood corpuscles are seen in the straight tubules. In the protoplasm of many of the cells lining the collecting tubules are seen brownish particles of pigment."

Schüller reviews the literature of cases similar to this, and accepts only two in which careful examination of the excised kidney failed to reveal any pathological affection. He thinks it is better to refer to these two cases as "unexplained" rather than to draw from them the general conclusion that hemorrhage may occur from a perfectly healthy kidney. The varied pathological findings in other cases he groups under seven headings. Congenital malformations, diffuse unilateral nephritis, diffuse or circumscribed unilateral nephritis, glomerulonephritis, fibroid degeneration of the capsula adiposa, mechanical lesions and their effects, and, lastly, a special group for the case described by Abbé, apparently due to calcareous incrustations in a papilla. The purely vasomotor theory advanced by Klemperer to explain the hemorrhage he receives with little favor, and inclines to the view of Albarran, that no matter what role the nervous system may play careful examination will practically always reveal some organic lesion however insignificant. He does not think that we can disregard this lesion on the assumption that it is altogether out of proportion to the clinical manifestations. The exact mechanism of the hemorrhage in these cases remains unexplained.

The Leishman-Donovan Body and Tropical Splenomegaly.—In November, 1900, LEISHMAN observed at the Royal Victoria Hospital, Netley, some curious bodies in smears from the spleens of individuals, who had been invalided home suffering from "Dum-dum" fever. His description did not appear until May, 1903 (*British Medical Journal*, May 30, 1903, vol. i. p. 1252). The name "Dum-dum" was applied to this tropical fever owing to its having extensively prevailed in a cantonment in India of that name. Nearly all the literature on these parasites has appeared in the *British Medical Journal* for the remainder of 1903 and up to the present date in 1904. Donovan's name is associated with these bodies owing to the fact that he was the first after Leishman to find them in the smears from the spleen in tropical cachexia. He was the first also to find them in the blood smears from the spleen obtained by splenic puncture *intra vitam*. At the recent meeting of the British Medical Association (*British Medical Journal*, September 17, 1904, pp. 642–658) the relationship of these new bodies to tropical splenomegaly and cachexia was thoroughly discussed in the Section on Tropical Diseases.

Briefly stated, the Leishman-Donovan bodies are demonstrable by

the Romanowsky stain or some of its modifications. They are small oval bodies 3 to 8μ in diameter. Each possesses two nuclei, one much larger than the other and oval in outline. The small nucleus is in the form of a small rod set perpendicularly or at a tangent to the larger one. The protoplasm of the body stains a reddish tint. They usually occur singly or in twos, but occasionally they are grouped together to the number of twenty, embedded in a matrix. It is now conceded that this grouping is due to their being contained within the bodies of macrophages. The bodies are not contained within the red corpuscles, although Laveran holds that they are. There is no authentic evidence of their having been found in the peripheral circulating blood. They have now been observed in a very large number of cases of tropical cachexia and splenomegaly in the splenic blood obtained *intra vitam*.

Clinically the cases present the following symptoms: Irregular remittent or intermittent type of fever; grave anæmia of the secondary type; marked cachexia; progressive emaciation; and great enlargement of the spleen. Occasionally there is a history of dysentery. Most of the cases had previously been regarded as malarial in origin. What is of great interest is the fact that Bentley has shown that the disease known as "kala-azar," of Assam, presenting in general the symptoms enumerated above, is due to infection with this parasite. Homer Wright and others have demonstrated that the disease known as "Delhi boil" is caused by the same organism. It has been shown that the disease produced by the organism is widely distributed. It has been found in various parts of India, and has been observed in Omdurman, in lower Egypt, and in Tunis.

In addition to being found in the spleen it has been demonstrated in the liver, kidneys, mesenteric glands, walls of intestinal ulcers, and in lesions of the skin including those of "Delhi boil" and scabies. The disease is very fatal. Quinine is nothing like so efficacious as a curative agent as in malaria. Some observers claim that the drug is a prophylactic. The mode of entrance of the parasite into the body has not been ascertained. It is thought probable that it enters by way of the skin. So far it has not been found in the urine or feces of infected individuals. The Indian physicians now do splenic puncture as a routine in all cases of splenomegaly and apparently meet with no untoward sequelæ. The cases usually show a leukopenia and the differential count reveals a marked reduction of the polymorphonuclears, and an enormous increase in the lymphocytes and particularly in the large mononuclears.

Various views have been advanced as to the nature of these bodies. Leishman though that they were involution forms of the human trypanosome, but his view has been strongly opposed. In the hundreds of cases now on record no trypanosomes have been found in the circulating blood. Marchand and Leddingham supported Leishman's view. Laveran, who studied Donovan's specimens, thought that it was a form of piroplasma similar to the piroplasma bigeminum, the parasite of Texas cattle fever, and that they were sometimes contained in the red cells. Ross, supported by the majority of observers, thinks that we have to deal with an entirely new genus of the sporozoa.

The suggestion has been made that the splenomegalies of splenic anæmia and Banti's disease may be due to infections with this parasite. Additional interest is thus added to these diseases in this country.

Removal of the Biurate Deposits and Excision of the Articular Capsule in Gouty Arthritis of the Big Toe Joints.—RIEDEL (*La Semaine Médicale*, October 5, 1904), of Jena, reports two cases in which this operation was performed in gouty patients, with excellent results. He operated on his first case in 1882. The patient was a man, aged forty-five years, who was suffering from an attack of gouty arthritis of the right big toe joint. He remained perfectly well until 1896 without any recurrence of gouty attacks. In 1897 he had a vertebral arthritis and died of some unknown cause. The second case was a woman, aged seventy years, on whom he operated in 1894. This was her initial attack of gouty arthritis, which also affected the right big toe joint. There was never any return of the arthritis, the patient dying of aortic stenosis in 1902.

In both cases Riedel suspected that he was dealing with an acute suppurative bursitis in which the bursa communicated with the cavity of the big toe joint. He was surprised to find that it was actually a gouty arthritis with extensive deposits of biurates in the bursal sac and joint capsule. The bursa and entire joint capsule were excised in both cases, the ends of the bones not being removed. The edges of the incision were brought together but not sutured. Healing was perfectly satisfactory. The operation is recommended only for cases where the gouty attacks have been confined to the big toe joints. It is contra-indicated in a polyarthritis.

Studies on the Tuberculin Reaction.—TRUDEAU, BALDWIN, and KINGHORN (*Journal of Medical Research*, August, 1904, vol. xii. p. 169) have carried out a series of experiments on guinea-pigs and rabbits, which are much less susceptible to tuberculin than human beings, with the object of better understanding the nature and specificity of tuberculin. Regarding the effect tuberculin has in spreading tuberculosis, they find that there is no such tendency in the case of corneal tuberculosis of the rabbit's eye, but that, on the contrary, as they had previously observed, there was a favorable absorptive influence on the diseased focus. Extirpation of a tuberculous focus was followed by loss of reaction—susceptibility to tuberculin. They conducted a series of experiments to ascertain whether specific tubercles are necessary for a positive reaction. Berkefeld filter capsules containing tubercle bacilli were introduced into the peritoneal cavity of rabbits. These capsules prevented the bacilli from coming into direct contact with the tissues, but by dialysis permitted the soluble products of the bacilli to pass through these walls. Some time after these had been introduced the animal was injected with tuberculin. It was found that the dialysable products failed to produce any local reaction about the capsules and the temperature elevations gave no certain evidence of susceptibility of these animals to tuberculin. The writers conclude that the presence of tubercle bacilli or substance in the tissues appears necessary to a true tuberculin reaction. The latter is apparently not due to the action of an enzyme. In support of this view is the fact that injections of trypsin failed to produce reactions when injected into animals with tuberculous abscesses. The tuberculin reaction may begin as early as the fourth or fifth day after infection with tubercle bacilli, but is constant after the thirteenth or fourteenth day. They were not able to conclusively demonstrate what constituent of the tubercle bacillus is responsible for the occurrence of the tuberculin reaction.

THERAPEUTICS.

UNDER THE CHARGE OF

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ASSISTED BY

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Results of Radiotherapy in Leukæmia.—DR. FRIED has treated two cases of leukæmia by this means and has produced a considerable improvement in both. The patients were forty-six and fifty-nine years of age. Under the *x*-ray the white blood cells, which had been 62,000 in one case and 132,000 in the other, became normal or nearly so. The red cells and hæmoglobin were increased. The spleen diminished in size. The general condition improved, and in one case the weight was increased. These results were obtained in a short time and were such as no other treatment has been able to give. There were no unpleasant after-effects worthy of notice.—*Münchener medizinische Wochenschrift*, 1904, No. 40, p. 1772.

The Serum Therapy of Typhoid Fever.—PROF. CHANTEMESSE gives as the mortality in typhoid fever treated by his serum 4 per cent. The statistics are from 523 cases observed from April 1, 1901, to October 26, 1904. He has collected the statistics of 2618 cases treated at various hospitals in Paris, and finds the mortality to be 18 per cent. He replies to the statement made by some, that his good results are due rather to hydrotherapy than to the serum, by the assertion that where baths alone are used, the statistics show a mortality of 18 per cent. In 1902 he stated that serum therapy in connection with proper bath treatment should reduce the mortality from typhoid fever to 4 per cent. or 5 per cent., and, in the light of the results obtained since that time, he sees no reason to change his opinion. The serum employed is obtained from horses immunized by injections of a soluble typhoid toxin. Under the administration of the serum he considers that the liability to intestinal perforation is diminished from 2.6 per cent. to 1.6 per cent., and he has never observed perforation in a case injected before the seventh day of the disease. An interesting fact in connection with the serum treatment is that the agent should be given in smaller doses to the severe cases than to those of the ordinary type.—*La presse médicale*, 1904, No. 86, p. 681.

Cryogenin and Typhoid Fever.—DR. BOUTTEVILLE (*Thèse de Paris*, 1904) believes that the bath treatment is the method of choice, but if the baths are contraindicated or ineffective, we may have recourse to antipyretics. The author gives the results of a series of cases in which cryogenin was used. The drug was administered as follows: 15 grains on the first day, 9 grains on the second, 6 grains on the third, then from 3 to 6

grains daily, depending on the effect produced. Under this treatment the dryness of the tongue, the vomiting, and the nervous symptoms, nervousness, insomnia, stupor, and delirium disappeared. The cryogenin was given only in rebellious cases. In 14 out of 21 cases defervescence took place upon the twelfth day or earlier. In the others the fall of the temperature was more marked when a cold bath or a dose of quinine was preceded by the administration of cryogenin. The temperature would remain down for some hours. The author believes that one may use this drug in connection with bathing and hold the temperature in check better than when it is not given, that it will ameliorate the general condition and hasten defervescence, and that it is the drug of choice when baths are contraindicated. No bad effects were noticed due to its use, and it has a very certain effect in the fever of convalescence. —*Revue de thérapeutique*, 1904, No. 21, p. 735.

Fresh Air in Nervous Cases.—Dr. Van Oordt considers that treatment by means of rest in the open air, like that prescribed in tuberculosis, gives excellent results in the nervous complications of the infectious nervous disorders of digestion accompanied by emaciation; insomnia, cardiovascular neuroses, medullary irritability, and tabes are also indications. In hysteria, neurasthenia, neuralgia, migraine, and obsessions this treatment is without result.—*Zeitschrift für diätetrische und physikalische Therapie*, 1904, No. 5, p. 281.

Pulverized Antitetanic Serum in the Prophylaxis of Tetanus.—M. Letulle employs upon every suspicious wound a dressing prepared as follows: After thorough disinfection of the lesion it is plentifully sprinkled with dry pulverized antitetanic serum and covered with a protective dressing of sterile cotton or gauze. The dressing is allowed to remain twenty-four hours, and if suppuration takes place it should be renewed as above until all pus has disappeared. The procedure has no disadvantages, it is not followed by erythema or arthralgia, and, in view of its simplicity and the results attained, the author believes that it should be employed as a routine on all wounds that have any possibility of having been infected with tetanus.—*La presse médicale*, 1904, No. 57, p. 452.

Diphtheria Antitoxin in Ozæna.—Dr. Tarnowski has succeeded in arresting a beginning case of this affection by a single injection of 1500 units of antitoxin. In a second case, which had been treated by sodium sozo-iodolate for a considerable period without effect, 1500 units in eight days produced a permanent result. In a third case of forty years' standing no definite success was attained, but the production of crusts was lessened to a great extent. The author considers that this method of treatment is worthy of further trial.—*Deutsche medicinische Wochenschrift*, 1904, No. 23, p. 850.

The Serum Therapy of Rheumatism.—Dr. Schaefer has observed the effects of Menzer's serum in six cases. None of these was subjected to any other form of treatment. In most of the cases the injection was followed by some pain and urticaria. These symptoms were, however, not of sufficiently unpleasant character to necessitate a cessation of the treatment. In four of the patients the disease was in the chronic

stage, and the serum wrought a cure within five days. No bad effects upon any of the bodily functions were noticed. In a boy, aged thirteen years, with a rheumatic mitral insufficiency, the cardiac symptoms were greatly relieved. The quantity of serum administered was from 15 to 75 minims every two days, depending upon the age of the patient and the reaction produced.—*Die Therapie der Gegenwart*, 1904, No. 3, p. 106.

Sodium Biborate in Epilepsy.—Dr. F. Hoppe finds that in certain epileptics the bromides do not yield good results, and are not well borne, because of complications such as renal insufficiency, circulatory disturbances, or digestive disorders, especially hyperchlorhydria. In such cases he has used borax, and to twelve patients he has given from fifteen to forty-five grains a day. From his results he concludes that borax is unquestionably contraindicated where any insufficiency of the organs of elimination is present. In five of the patients very good effects were noticed. In one of these, a corpulent individual, suffering also from anæmia and hyperchlorhydria, the condition was materially improved, the seizures became more rare, and the body weight became less. On this patient alone did the drug act as a diuretic. The patients were given five grains three times a day with no unpleasant effect. Borax was also tried for six weeks in cases of uncomplicated epilepsy, but no amelioration was noted, and the bromide treatment was resumed. In conclusion, the author affirms that borax has no specific action in epilepsy, but may act well in cases complicated with gastric disorders, especially hyperacidity.—*Berliner klinische Wochenschrift*, 1904, No. 27, p. 730.

Mercurial Injections in Syphilis.—Dr. Leredde advises in cases of syphilis which resist moderate doses of mercury and will tolerate the drug in large quantities, the use of the benzoate or the biniodide, $\frac{3}{10}$ to $\frac{1}{2}$ a grain hypodermically. This dosage, carefully increased, is unlikely to cause stomatitis and obviates the inaccuracy and inconvenience of inunctions. The author asserts that the use of injections should always be the treatment of choice in syphilis.—*Revue pratique des maladies cutanées*, 1904, No. 6, p. 186.

Theocin-sodium Acetate.—Dr. J. Meinertz, after experimenting with this agent upon a series of patients, concludes that it is of considerable value in properly selected cases, especially in œdema and dropsy of cardiac origin. In order to get its best action there must be a considerable blood pressure, consequently in many cases its employment in combination with digitalis is advisable. This salt seems to be less likely to be attended by unpleasant after-effects than theocin.—*Therapeutische Monatshefte*, 1904, No. 6, p. 275.

Rheumasan.—Dr. F. Kobisch employs this agent, which is a 10 per cent. of salicylic acid ointment in superfatted soap, in various painful chronic conditions, such as polyarthritis, sciatica, lumbago, tabes dorsalis, gout, and neuritis, in the following manner: About 2 drachms are thoroughly rubbed into the affected part, which is then covered with a thin layer of cotton, which, after twelve hours, is removed. The skin is then washed, but not entirely dried, and a second inunction

is given. This procedure is repeated night and morning for two days, and after a two-day interval is renewed. In a few cases an irritation of the skin is produced. That the salicylic acid is absorbed is proven by the fact that it may be demonstrated in the urine about four hours after a treatment.—*Deutsche medicinische Wochenschrift*, 1904, No. 38, p. 683.

Internal Treatment of Pleurisy with Effusion.—Dr. Lewaschew states that it is not rare to observe an arrest of the disease following the observance of proper hygiene and the suppression of the causes predisposing to the inflammation. He regards the use of counter-irritant local applications as useless in most cases as far as favoring the absorption of the fluid is concerned. With regard to internal treatment he considers the salicylates to be most effective in limiting the inflammation and causing the absorption of the fluid. Sodium salicylate is the preparation of choice and if it does not produce the desired result in two or three weeks more active treatment is necessary, that is to say, thoracocentesis. The dosage of sodium salicylate recommended by the author is 7½ to 12 grains, four to six times a day, or less than this quantity in women or feeble patients.—*Wiener Medicinische Presse*, 1904, Nos. 37 and 38, pp. 1741 and 1797.

Hetol in Pulmonary Tuberculosis.—Dr. T. Barrett Heggs cites 7 cases which were treated by intravenous injections of hetol (synthetic sodium cinnamate). In all of them the tubercle bacillus was present in the sputum. Two of the cases were injected for about six months and the others for six or seven weeks. The blood for counting was taken four hours after a meal on alternate days in each case. The technique of the injection was simply to be certain that skin and instruments were surgically clean and to inject the drug into any sufficiently large vein of the arm. The method of graduated increase of dose on alternate days was followed and the maximum dose varied from 20 to 50 milligrams, never getting any ill effects. The leukocytosis was not in proportion to the amount of the injection. The maximum leukocytosis was generally obtained with about 20 milligrams. In all cases the injections were followed by definite leukocytosis. Often the normal count was doubled. In every case marked improvement followed the treatment, although some of the patients were taking creosote and cod-liver oil as well as the injections of hetol. The author's results lead him to the opinion that this remedy, though not a specific, is a useful adjunct to any other treatment of tuberculosis.—*Lancet*, 1904, No. 4234, p. 1136.

Mercurial Inunctions in Syphilis.—Dr. N. P. Fetschenko after experimenting upon 150 patients with different mercurial ointments with the idea of reporting upon their absorption, states less of the unguent is absorbed than one would suppose. Of blue ointment, for instance, about 25 per cent. is absorbed and that of a preparation not made up with lanolin. Freshly made ointments and those containing lanolin are very feebly absorbed. Resorbin and vasogen, especially the former, are excellent vehicles. It is useless to prolong the rubbing more than one-half an hour or to increase the quantity of the ointment beyond a certain point. The skin will absorb just so much and no more. The

skins of those who wash frequently have the best absorptive powers, and absorption is at its maximum after a hot soap and water bath. In summer absorption is more active than in winter and energetic friction as well as the addition of gaultheria or menthol added to the ointment aids absorption.—*Wiener Klinisch-therapeutische Wochenschrift*, 1904, No. 15, p. 419.

Physical Methods in Treatment of Chronic Articular Rheumatism.—DR. N. DOHAN considers that too little attention is paid to physical methods in the management of this affection. He recommends that the diseased joint be subjected to an induced current for eight to ten minutes. This relieves the pain to a considerable extent. Then the joint is bathed in water at 58° to 60°, or swathed in bandages wet with cold water. After the pain has been benefited by these procedures an electric light bath, lasting from eight to ten minutes is prescribed, followed by a cold douche to the joint. After this the joint should not be dried immediately. During the treatment a more or less rigid milk diet is advised.—*Blätter für klinische Hydrotherapie*, 1904, No. 9, p. 197.

Antistreptococcus Serum in Puerperal Sepsis.—DRS. H. PILCER and M. EBERSON conclude a study of the effect of this agent upon 28 cases with the following statements: 1. That Marmorek's antistreptococcus serum is not a specific against all forms of puerperal sepsis, but it is a powerful adjunct to other treatment of this infection. 2. The serum acts by stimulating the formation of leukocytes in the diseased organism, and for this reason it is indispensable in puerperal fever. 3. The serum produces a feeling of well-being in the patient which is a point in favor of its administration in connection with other therapeutic agents. 4. To produce the best effects the serum must be injected in sufficiently large quantity, the average dose being from 1½ to 3 ounces.—*Therapeutische Monatshefte*, 1904, No. 10, p. 509.

Age Limits in Cold Water Therapy.—DR. WINTERNITZ protests against the prejudice which exists against the employment of cold water in anæmic and debilitated persons on the ground that it extracts body heat. On the contrary, according to him, the cold water augments the production of heat. In infants cyanotic and cold from gastro-enteritis he has obtained remarkable results by means of friction with cloths wrung out in cold water. Such applications provoke a considerable excitation of the organic functions and are indicated in the infant in all torpid conditions and circulatory disturbances. He considers extreme youth no contraindication to the application of cold water. Likewise in old age he recommends rapid local use of cold water. Arteriosclerosis is no contraindication. At first sight this would not seem true for cold increases the blood pressure, already below normal in atheromatous patients. The author recognizes two varieties of arteriosclerosis, one with increased blood pressure, the other, and these are the more gravely affected, with an arterial pressure below the normal. But quick applications of cold lower the pressure in the first group and elevate it in the second; in the former class the hydrotherapy stimulates inhibition, in the second it excites the organism.—*Blätter für klinische Hydrotherapie*, 1904, No. 8, p. 173.

PEDIATRICS.

UNDER THE CHARGE OF

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Heart Complications in Diphtheria. A Clinical Study of 946 Cases.—FRANKLIN W. WHITE and HOWARD H. SMITH (*Boston Medical and Surgical Journal*, 1904, vol. cli., No. 16) give their clinical observations of nearly 1000 cases of diphtheria treated at the Boston City Hospital during one year. The cases were studied principally to determine the character and frequency of heart lesions and their practical importance in prognosis and treatment.

About 5 per cent. were less than one year of age, 40 per cent. less than five years, and about 70 per cent. less than ten years old. In one-quarter of the cases the illness was severe; more than one-half of these, or 132, proved fatal. Only a fourth of the deaths were from heart complications; the most frequent cause was bronchopneumonia following intubation or tracheotomy. These facts are opposed to Villy's statement that the majority of fatal cases of diphtheria die on account of heart complications.

The patients came mainly from the poorer classes, where treatment is likely to be deferred, so that most of them did not receive antitoxin until the second or third day; and of the severe and fatal cases, at least two-thirds were four, five, or more days without antitoxin treatment.

The symptoms and physical signs of cardiac disturbance are treated at length. About 60 per cent. of the cases showed irregularity of the pulse. This sign was more frequent in the younger patients, and was observed in the severe, moderate, and even mild cases. It was very variable in its appearance and duration. The rhythm would change from marked irregularity to perfect regularity often within half an hour.

The number of patients with heart murmurs is a striking feature of the study: 878 had heart murmurs at either the apex or base, or 94 per cent. of the cases where the condition of the heart was carefully observed and recorded. These murmurs were not faint or doubtful, but for the most part were loud and blowing, and in each case were confirmed by two or three competent observers. The murmurs were all systolic in time, with the exception of those in a few cases of chronic heart disease. They were usually heard at the apex, frequently transmitted to the axilla, and associated with accentuation of the pulmonic second. The majority were accompanied by irregular heart action and outlasted the fever. In 90 per cent. of the patients with murmurs, this sign was present upon entrance to the hospital, and in about 78 per cent. of the cases one or more murmurs were present at discharge. The duration

of the murmurs after leaving the hospital is unknown, except in a few instances. Five or six of the patients were examined some eight months after their discharge, and each showed a murmur; two of these, in addition, having cardiac enlargement and evidences of myocarditis.

As to prognosis, the author believes that the mere presence of a murmur has little of value, as the sign is so nearly universal.

The clinical course of the cases does not explain the cause of these murmurs. Pathological studies show that they are probably due largely to relative mitral insufficiency resulting from changes in the heart muscles, or to changes in the innervation of the heart. Autopsies have shown that endocarditis and pericarditis are extremely rare complications of diphtheria. Cardiac enlargement was infrequent, and was found only in the severe cases. The writers believe that the frequency of acute dilatation and syncope has been exaggerated, as almost all of their fatal cases showed a gradual heart-failure. They agree with Poynton that dilatation of the heart is not so marked in diphtheria as in rheumatic fever.

In the patients with chronic heart disease, 17 in number, the course of the illness was no more severe than in the average patient.

The cases with heart complications are divided into three separate types. The first and most serious type have gallop rhythm, vomiting, epigastric pain and tenderness, run a short course of two or three weeks, and die in the majority of cases. The second type lasts for weeks or months, with a rapid, regular, or irregular heart, easily affected by slight exertion, and gradually becoming normal in rate. There are few other important symptoms. The third type is rare; its main feature is a very slow pulse, occurring at the end of the second or the beginning of the third week. There is a marked decrease in rate over a period of three days, the pulse dropping from 110 or thereabouts to 30 or even 20. The subjective symptoms are slight until the pulse reaches a low level (40), when signs of prostration set in. The sounds are weak, and a moderate degree of dilatation occurs. There were 3 such cases in the series, all fatal; 36 of the cases were considered as having serious heart complications. Two-thirds of these patients died. Four-fifths of the fatal cases had no treatment until after the fourth day.

The most important cardiac symptom is gallop rhythm; this was found in all the 36 cases. The murmurs usually become indistinguishable upon the appearance of this symptom.

Late vomiting is the next important symptom. It was present in all but 4 of the fatal cases. In nearly every case the appearance of the gallop rhythm preceded the onset of vomiting from one to four days.

The next symptom is epigastric pain and tenderness. Nine-tenths of the patients who had this symptom died. This symptom usually was closely associated in time with the appearance of vomiting, either a day or two before or a day or two after.

Palatal paralysis was noted in 19 of the severe cases and in 10 of the fatal cases.

The importance of these symptoms (gallop rhythm, late vomiting, epigastric pain and tenderness) as danger signals and their value in prognosis are shown by the fact that they were very frequent in the severe and fatal cases, and very rare in those that recovered.

As to the treatment, rest in bed is considered of most importance in dealing with heart complications. The figures show that the serious

complications nearly always develop within three weeks from the onset of the illness. Mild cases are allowed to be out of bed at the end of two weeks. The presence of murmurs and a slight degree of irregularity are no contraindication if the first sound is strong and the heart is not dilated.

The severe cases must be watched for four or five weeks, but after this time the danger from serious heart complication is usually over. In cases with gallop rhythm, absolute rest in bed, upon a liquid diet, is necessary. At the first appearance of vomiting food should be given by rectum. Strychnine gives the best results. Alcohol and digitalis are not well borne. Morphine may be necessary. The after-treatment of all except the mild cases consists in watching the effect of mild exercise upon the heart for several months, and grading it to meet individual requirements.

OBSTETRICS.

UNDER THE CHARGE OF

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Spontaneous Rupture of the Uterus after Cæsarean Section.—KERR (*British Medical Journal*, June 18, 1904) reports the case of a patient upon whom he had previously performed Cæsarean section, employing the transverse incision across the fundus. The patient was not sterilized. She was admitted to the hospital in a succeeding pregnancy, estimated at the thirtieth week. She was given an enema, after which she complained of pain in the abdomen, but shortly afterward fell asleep. The next morning the pain extended over the entire abdomen, tenderness gradually developed, the pulse rose to 90, the temperature became subnormal, and the breathing more rapid. The patient lay with her feet slightly drawn up, and the fetal parts could be felt with great distinctness through the abdominal wall. There was some blood-stained vaginal discharge.

On performing abdominal section a large quantity of dark-colored blood escaped, and the fœtus and placenta lay in the abdomen with the membranes unbroken. The uterus was retracted behind the fœtus, and had a transverse rupture through the scar of the previous operation. Hysterectomy was performed, leaving a stump of cervix, and the patient made a good recovery.

Cæsarean Section for Contracted Pelvis.—At a recent meeting of the Obstetrical Society of London (*British Medical Journal*, October 22, 1904), KERR based his paper upon 30 cases of Cæsarean section. His maternal mortality was 6.6 per cent. His morbidity based upon a temperature of 100.5° on more than one occasion was 26 per cent.

Of the two cases fatal, one died on the fifth day from septic peritonitis, the other the day after the operation from the parting of several uterine stitches with free bleeding. He believed that if a patient came under the care of the physician sufficiently long to receive thorough preparation, celiohysterotomy should be done. Where, however, time for preparation is scanty and the condition of the uterus uncertain, celiohysterectomy is the operation of choice.

Hermann believed that early operation was very safe and late operation dangerous. Griffith had lost a case in Cæsarean section and did not think vaginal douches proper unless there was distinct evidence of infection. Where sterilization was desired he ligated the tubes with fine silk. Routh would allow the patient to choose the method of operation and if sterilization was admissible, he would accomplish it by removing the uterus, leaving the ovaries. Spencer had performed eight operations without mortality.

The Bladder and its Disorders During the Puerperal Period.—In the *Monatsschrift für Geburtshülfe und Gynäkologie*, 1904, Band xx., RUGE contributes an interesting paper upon this subject.

Writers have formerly ascribed most disturbances in the bladder after labor to overdistention. Some have given abdominal pressure undue importance. His researches led him to believe that the mechanism of labor is such in all cases where the child is delivered through the vagina, that strong pressure is brought to bear upon the bladder at the neck and trigonum, and that this pressure causes lesions which produce characteristic results. The longer the labor, the greater the pressure. The proportionate size of the head and pelvis, the length of time that the head is in the pelvis and especially the length of time that the head remains upon the pelvic floor are important factors. The longer the expulsive stage of labor, the greater the danger of injury to the bladder.

The anatomy of the bladder is such as to produce the characteristic lesion described as bullous œdema. In other cases œdema of the bladder wall is frequently found. Areas of darkened color with swelling of the mucous membrane are observed by the cystoscope and persist from four to six weeks after the birth of the child.

Hemorrhage may also occur from the sphincter of the bladder to the posterior wall. Such hemorrhage is beneath the epithelium, its areas of various shapes. The color changes during the process of recovery.

When his cases are reviewed, it is found that lesions of the bladder are not confined to those cases of labor terminated by difficult obstetric operations. Pelvic contraction was not present in these cases. Where injuries were but slight, no symptoms were present; where they were severe, the patient had retention of urine or painful micturition. Changes in the urine were present, dependent upon the altered condition of the mucous membrane of the bladder. The bladder was especially liable to infection and hence the utmost precaution in the use of the catheter was imperative. Lesions of the ureters and urethra, similar to those found in the bladder, were also observed.

Lithopædion Forty-one Years in the Abdominal Cavity.—In the *Journal of Obstetrics of the British Empire*, October, 1904, HAULTAIN reports the case of a patient dying of cardiac disease who had within the abdomen a lithopædion forty-one years.

On post-mortem examination, the calcified fœtus was found behind the uterus, densely adherent to the intestines and surroundings. The head was downward and there was no enveloping sac. The uterus was atrophied and adherent to the front of the fœtus. The patient was well aware of the presence of the child and had frequently remarked upon it. She had occasional attacks of abdominal inflammation, but was usually in good health.

The fœtus was in the usual attitude, the limbs were in absolute preservation, the nails projected over the finger-tips. On the back, scalp, and breech the tissue seemed to be of normal thickness.

The Albuminuria of Pregnancy.—In the *American Journal of Obstetrics*, September, 1904, LITTLE gives the results of the examination of urine in pregnant patients in the obstetric wards of the Johns Hopkins Hospital. Although the records of 960 cases were available, they were not considered sufficiently exact for purposes of investigation. The urine was examined in 100 consecutive cases in the most minute and painstaking manner and the results are stated.

In catheterized specimens of urine from about one-half of all pregnant women, equally in primiparæ and multiparæ, albumin is found. In urine which is voided, albumin is more frequent in the cases of multiparæ. Casts are more often found in the urine of multiparæ. Labor produces a decided increase in albumin alone and casts and albumin especially in primiparæ. The increased blood pressure and muscular contraction of labor account for this. Casts without albumin are often found during pregnancy, labor, and the puerperal state. In the puerperal state, albumin and casts occur less frequently than in pregnancy. In no case was albumin present during pregnancy and absent at the time of labor, while casts during pregnancy and absent at the time of labor were found in only three cases. Two-thirds of the cases which showed casts at the time of labor had albuminuria during pregnancy.

As regards the pathological conditions attended by the presence of albumin it was found in 25 cases of eclampsia and 9 cases of threatened eclampsia. When eclampsia occurred, casts were present in 22 out of 23 cases. Pernicious nausea showed much albumin and many casts. During the puerperal period, albumin and casts persisted longest in those cases in which they had been found during pregnancy. Albuminuria was present in 4 cases of abortion, 2 from syphilis, 1 from typhoid fever, and 1 from chronic nephritis. Albuminuria without complications did not in any case produce abortion. Nausea and vomiting was present in 20 per cent. of primiparæ and 33⅓ per cent. of multiparæ who at some time had albuminuria. Œdema was present in one-third of these cases.

So far as the association of albuminuria with renal disease is concerned, it is pointed out that the albuminuria of pregnancy is the result of a toxæmia and not of a true nephritis. The kidney of pregnancy is the result of a degenerative process, resulting from the circulation of blood laden with toxins through the kidney.

Spontaneous Rupture of the Pregnant Uterus through the Scar of a Former Cæsarean Section by Transverse Incision.—In the *Zentralblatt für Gynäkologie*, 1904, No. 44, EKSTEIN reports what he describes as the first spontaneous rupture of the scar occurring after this operation.

Regarding the condition of the scar after Cæsarean section, there are various observations: Brünings, in a repeated Cæsarean section, found the scar of the first operation greatly thinned. Gueniot, seventeen months after a Cæsarean section, found stitches still remaining in the scar. Two years after Cæsarean section Everke found no stitches in the scar. Czyzewicz, four years after a Cæsarean section, in performing a second, found the scar white and glistening and the anterior uterine wall greatly thinned. Three and a half years after Cæsarean section Rühle found the scar of the former operation so thin that he performed hysterectomy. Lihotzsky, seven years after Cæsarean section, found that silk sutures had been completely absorbed. Brown and Saenger believe that in sixty days after operation the greater part of silk stitches are absorbed. Schneider found, two years after Cæsarean section, no trace of the former scar. Staude, two years after operation, found the scar of the first a narrow white line and no silk sutures remaining. Löhlein performed 3 successful Cæsarean operations upon the same patient. He observed no tendency to dilatation of the scar. These operations were performed by the longitudinal incision.

Regarding the scar in the transverse incision, Ludwig found silk sutures in the scar one and a half years after operation. Flateau, two years after operation, could find no trace of sutures in the transverse incision. It is evident from these reports that the scar after operation differs greatly in different cases. Spontaneous rupture through the scar is, however, of rare occurrence. Woyer reports a case of spontaneous rupture in a uterus pregnant, with twins, in a patient on whom Cæsarean section had been performed three years previously. The uterus had been closed by thirty silk sutures. Guillame observed rupture through the scar of a former Cæsarean section three years after operation, occurring at the seventh month of pregnancy. Targett reports a case of rupture through a Cæsarean scar. Everke exhibited a uterus with spontaneous rupture through a Cæsarean scar, the operation having been performed four years previously by the Saenger method. In this case the entire scar separated and the placenta was found in the point of rupture. Meyer reports 2 cases; in the first, rupture of the abdominal and uterine wound on the ninth day after operation, the patient recovering; in a second operation on the same patient two years later there was no trace of the scar of the first operation. A longitudinal incision was again made, closed with eight silk sutures, with good result. In a second case, Cæsarean section had been done for contracted pelvis and the uterus closed with catgut suture. Two and a half years afterward a second operation was done, and rupture in the old scar was found with some protrusion of placenta.

There is reason to believe that the attachment of the placenta over the scar favors the occurrence of rupture. Some have thought that the anterior incision is less likely to rupture, because adhesions frequently occur between the uterus and abdominal wall, thus strengthening the uterine wall at this point.

Ekstein's case is as follows: The patient, aged thirty-three years, was in her fourth pregnancy. The first and second pregnancies were terminated by craniotomy. The third ended by Cæsarean section, and the patient was advised for subsequent pregnancy to return to the hospital for the induction of labor. At nine months' gestation after exertion the patient was brought to the hospital, stating that she had felt no

movements of the child for two days. On examination the patient was evidently in the ninth month of gestation; the abdomen was greatly distended, so that a thorough examination was impossible. Neither heart sounds nor uterine souffle could be heard. The abdomen was very sensitive on pressure. The heart and lungs of the mother were practically normal, although the pulse and respiratory rate were increased. The tongue was heavily coated, and there was frequent vomiting of a greenish-yellow mucus. The patient's temperature was practically normal. The vomiting and abdominal distention increased, and the pulse rose to 140. Upon operation decomposed blood was found in the abdomen, the child had entirely escaped with its appendages through the uterus, the placenta lay upon the right side, the child with its back toward the left and posteriorly, the head near the left iliac bone. The uterus had firmly contracted and the scar of the former Cæsarean section had completely ruptured and a portion of the membranes remained within the rupture. The child was dead, the amniotic liquid a brownish-gray and discolored. The child and blood were removed from the abdomen and hysterectomy performed. The patient died shortly after the operation. Examination of the uterus showed that suture material had entirely disappeared from the scar. The placenta had been attached upon the anterior wall of the uterus and partially over the scar. Microscopic examination showed that the decidua extended over the entire laceration and upon the anterior wall. The uterus was remarkably firmly contracted.

The Cæsarean operation performed in the preceding pregnancy had been by the transverse incision at the fundus, silk had been used as suture material in the muscle, and catgut had been employed for peritoneal surfaces. This operation was performed about three years before the rupture of the uterus.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Lipoma of the Abdomen.—MICHEL (*Zentralblatt für Gynäkologie*, 1904, No. 41) reviews the literature of the subject thoroughly. He includes subcutaneous, intramuscular, pre- and retroperitoneal lipomata. The latter are of especial interest from a diagnostic standpoint, and are quite rare. The retroperitoneal variety is usually unilateral, developing either from the perirenal fat or between the peritoneal and abdominal wall in the iliac fossa, in the broad ligaments, or between the rectum and bladder. They may be sessile or pedunculated, single or multiple, and may reach an enormous size (twenty to sixty pounds). They are often so soft as to give the impression of fluctuation, hence

they have frequently been mistaken for ovarian cysts. They differ from the latter neoplasms in being less elastic and independent of the uterus, while the intestines lie in front of them or at one side, as in the case of renal growths. Peritoneal tuberculosis, cysts of the mesentery, and even the pregnant uterus may be confounded with lipomata.

The principal symptoms are those due to pressure on the hollow viscera and bloodvessels. The prognosis after operation for the removal of retroperitoneal lipomata is grave, only 4 recoveries having been reported out of 11 cases.

The pre-peritoneal variety develop between the peritoneum and transversalis fascia and grow into the abdominal cavity where they may become detached, so that it is difficult to distinguish them from hernia or fatty degeneration of the omentum. Through traction they may give rise to severe gastric symptoms. The writer reports an interesting case in which the diagnosis of ovarian cystoma was made. Various theories have been advanced regarding their origin, such as local disturbances of the circulation in the bloodvessels and lymphvessels, reflex nervous conditions, or aberrant cells (Recklinghausen). Local irritation, heredity and struma have also been stated to be etiological factors. A direct relation between thyroid hypertrophy and lipomata has been claimed by several observers. The writer inclines to Ribbert's theory of fetal inclusion. The only treatment is surgical, especially in view of the fact that sarcomatous degeneration has been noted in some instances.

Adnexal Disease Due to Typhoid Fever.—Dirmoser (*Zentralblatt für Gynäkologie*, No. 40, 1904) reports a case of tubo-ovarian abscess in a virgin who had typhoid six months before. The characteristic bacilli were found in the pus. A similar case was reported by Koch, who inferred that the infection came through the intestine. The writer believes that the bacilli make their way through the lymph channels in the gut to the surrounding connective tissue and thus reach the ovary and tube, though the possibility of hæmatogenous infection cannot be denied.

Patent Urachus.—Swirt (*Nederl. Tijdschrift v. Geneesk.; Zentralblatt für Gyn.*, 1904, No. 41) reports the following cases:

1. The patient, aged fifty-eight years, entered the hospital on account of retention of urine, while urine dribbled from the umbilicus. An artificial vesicovaginal fistula was established, when the urachus closed spontaneously, and later the fistula also.

2. A girl, aged seventeen years, had constant dribbling of urine from the navel, blood escaping from the same opening at every menstrual period. The edges of the fistula were split and a purse-string suture was inserted, followed by primary union.

3. A boy, aged one and one-half years, had eczema of the navel with a discharge of offensive urine; he had also a marked phimosis. Circumcision failed to cure the fistula. As there was diastasis of the recti muscles, the umbilicus was excised and the opening of the urachus was successfully closed with a purse-string suture.

Treatment after Curettement.—Oria (*Rev. de med. y cir, Madrid; Zentralblatt für Gyn.*, 1904, No. 41) believes that sufficient care is not

given to the after-treatment of the patient. She should be kept in bed for three weeks after the operation. In proof of this he reports 400 cases from Madrazo's clinic, in not one of which were there any complications, nor was a second curettement required.

Gynecology in Turkey.—R. RIEDER-PASCHA in a report of the Gülhane at Constantinople calls attention to the fact that gonorrhœa is less common in Mohammedan women than in those of other sects. In the treatment of gonorrhœal endometritis the best results were obtained by applications of nitrate of silver, argonin, and formalin.

Cases of cancer of the cervix were rarely seen in an operable stage.

Retrodisplacements of the uterus were often an accompaniment of gastroenteroptosis and movable kidney, which the writer attributes to the vegetarian diet and chronic constipation so common in Turkish women, and to the fact that they are allowed to leave their beds too soon after parturition.

Pessaries are regarded with aversion by both native physicians and patients. Fibroids were comparatively rare except in negresses (4.9 per cent. of 952 patients), and were only operated upon when there was profuse hemorrhage or rapid growth. Total extirpation was usually performed with a mortality of 14 per cent. (!)

Conservative treatment of adnexal disease was the rule, only three abdominal operations being performed.

The report states that "parametritis" is the most common pelvic affection in Constantinople, local massage being a favorite method of treatment. All the cases of mammary cancer were received in an advanced stage.

Ultimate Results of Abdominal Hysterectomy for Cancer of the Uterus.—FREUND (*Zentralblatt für Gynäkologie*, 1904, No. 42) presented at a recent meeting of the German Medical Congress a patient whose uterus he had removed for cancer of the cervix and corpus uteri by the abdominal route, being the first successful case of total abdominal extirpation. The writer stated that he had from the beginning favored this method, though the subsequent bad results had rendered vaginal hysterectomy more popular. The fact that the pendulum had swung backward was a proof that the ultimate results of the vaginal operation had not been satisfactory. The importance of removal of the lymph nodes had been fully demonstrated, but this had only emphasized the fact that Freund's original operation was the correct method.

The reporter thought that surgeons should not be discouraged by the fact that the primary mortality of abdominal hysterectomy was still rather high. More favorable results could be expected provided that proper care was exercised in the selection of incipient cases.

Döderlein (*Ibid.*) reported 73 cases of hysterectomy from October, 1897, to January, 1900, with 15.8 per cent. cured; 10 patients who had cancer of the body of the uterus were entirely free from disease. Since January, 1902, the reporter had performed only the abdominal operation (112 cases), 30 per cent. of the patients being free from recurrence. In 26 out of 65 cases of cancer of the portio vaginalis (24.3 per cent.) cancerous lymph nodes were removed; in 29 per cent. of the cases of cervical cancer, and in 9 per cent. of those of malignant disease of the body of the uterus.

The fact that infected nodes were present in only 2 out of 23 cases of corporeal cancer showed that the latter could be treated equally well by vaginal hysterectomy.

Mackenrodt (*Ibid.*) stated that he had obtained 44 per cent. of permanent cures up to 1901 by vaginal igniextirpation. Since then he had operated in 71 cases, with a primary mortality of 19.7 per cent.; 77.4 per cent. were free from recurrence at intervals of one to three years, and 70.8 per cent. of all his surviving patients were well. In the discussion which followed Veit called attention to the high primary mortality (15 per cent.), which was due not so much to defective technique as to the disease itself; it will doubtless be lowered by better antiseptic preparatory treatment.

Wertheim stated that his percentage of cures after four years was 18.2 per cent. His primary mortality was 17 per cent.

Double Mammary Cancer.—BECK (Inaugural Dis.; Abstract in *Zentralblatt für Gynäkologie*, 1904, No. 42) analyzes 61 cases, and concludes that cancer in the opposite breast is really a metastasis and not primary disease. Whether the lymph vessels connecting the mammæ serve as channels of infection or not has not been clearly demonstrated. The writer inclines to the view that cancerous emboli are carried from the original site of disease to the other breast, rather than to the theory of direct extension along the lymphatics.

Torsion of the Pedicle of Ovarian Cysts.—TRANGENHEIM (Inaugural Dis.; *Zentralblatt für Gynäkologie*, 1904, No. 42) in reviewing the statistics of Olshausen's clinic found that in 971 ovariotomies torsion of the pedicle was found in 8.2 per cent., while in 101 cases of parovarian cyst 7 per cent. had twisted pedicles. Only 3 fatal cases were recorded: one from intestinal obstruction and two from peritonitis. The latter were in a hopeless condition before operation, as 17 other similar, but less severe, cases were operated upon successfully.

Laparotomy for Ruptured Ectopic Pregnancy.—SEIDEL (Inaugural Dis.; Abstract in *Zentralblatt für Gynäkologie*, 1904, No. 42) analyzes 90 cases from the Berlin clinic, 52 of intraperitoneal rupture, 13 of tubal abortion and 15 undetermined. In 30 there was no vaginal hemorrhage whatever, and in only 2 was decidual membrane discharged. Menstruation was absent in 53 cases, delayed in 16, regular in 16, and scanty in 5. Laparotomy was the operation elected. The mortality was 14.4 per cent., 6.6 per cent. succumbing from the operation; 5.2 per cent. of the patients had a second extrauterine and 24 per cent. a subsequent normal pregnancy.

Perforation of the Uterus versus Sounding of the Tubes.—THOM (*Zentralblatt für Gynäkologie*, 1904, No. 36) believes that most of the cases reported under the head of introduction of a sound into a dilated tube were really those of puncture of the uterine wall. He finds that experiments on the cadaver and living subject alike prove that it is impossible to introduce a sound into a normal tube from the uterine cavity. Only 2 previously reported cases (Bischoff's and Floeckinger's) are authentic, and in each of these there was a fibroid uterus, as well as dilatation of the distal ends. He reports 2 others, which prove that only

under abnormal conditions is sounding of the tube possible. In order to accomplish this, not only must the ostium uterinum, as well as the cornu, be dilated, but the wall of the tube must be capable of sufficient resistance, and the uterine cavity must be enlarged and the organ laterally displaced by fibroids or interstitial pregnancy.

Adenomyoma of the Uterus.—MEYER (*Zentralblatt für Gynäkologie*, 1904, N. 37) reports a case in which he found two small nodules from the posterior wall of the uterus, which microscopically consisted of fibromuscular tissue containing numerous groups of glands. The neoplasm had no relation to the endometrium. As they were diffuse and could not be enucleated, the uterus was extirpated.

The writer inclines to Recklinghausen's theory that they developed from the primordial kidneys, though it was possible that they had their origin in the endometrium (before or after birth), in the proliferated serous epithelium, or in the epithelium of Gärtner's ducts.

Saenger Operations for Prolapsus.—SCHEIB (*Monatsschrift für Geb. u. Gyn.*, Band. xviii, Heft 5) reports 141 cases, in 16 of which vaginofixation or ventrofixation was performed. In 65 patients who were kept under observation, 60 per cent. were cured.

Disinfection of the Hands.—SCHAEFFER (*Monatsschrift für Geb. u Gyn.*, Band xviii,. Heft 5), from experiments with sublamin, found that a 1 per cent. solution possesses a stronger bactericidal action than a 10 per cent. He regards alcohol as the best disinfectant of all, and prefers to simply wash his hands with hot water and alcohol.

Adhesions of the Spleen and Uterus—IVANYI (*Szülés zet és Nögy.; Zentralblatt für Gynäkologie*, 1904, No. 37) reports the case of a patient, aged thirty-eight years, who had formerly suffered from malaria. She had a retroflexed uterus; attached to the left side of the fundus was a large, smooth tumor, the shape of the spleen. The diagnosis of dermoid cyst was made, and possibly wandering spleen. The latter was confirmed under anæsthesia. On opening the abdomen the enlarged spleen was found to be firmly adherent to the fundus uteri and omentum, with torsion of its pedicle. The adhesions were separated and ventrofixation was performed, the spleen being subsequently supported by a bandage.

Ovarian Cysts of Unusual Size.—SKUTSCH (*Zentralblatt für Gynäkologie*, 1904, No. 37) reports 2 cases of large ovarian cystomata, one weighing 83 and the other 100 pounds, both of which were successfully removed, the patients remaining in good health afterward. He adds that such large tumors are now rare, as they are usually recognized and removed early. It is only in women living in remote places in the country that they would be likely to grow so large.

False Ova in Cancer of the Ovary.—LIEPMANN (*Zeitschrift für Geb. u. Gyn.*, Band lii., Heft 2) calls attention to the fact that the appearances described by authors as persistent ova in cancerous ovaries are really products of degeneration, being cavities which contain bodies resembling primordial ova situated between the epithelial groups and processes.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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A Case of Choroidal Inflammation Caused by Excessive Use of the Eyes.—ST. JOHN ROOSA (*New York Medical Record*, February 20, 1904) reports the case of a physician, aged forty-six years, who, after ten hours of almost continuous reading of rather but not excessively small type, discovered the following morning a very disturbing blur confined to the right eye. He took a trip on the water and was exposed to the glare, taking no particular pains to prevent its influence on his eyes. The blur continuing, the patient consulted Dr. Roosa six weeks later (October, 1896). Vision: right, $\frac{2}{10}$; left, $\frac{2}{10}$. The vitreous of the right eye was so hazy that no good view could be obtained back of the fundus. He was not examined again until January, 1898, when the vision was found to be the same, the subjective blur persisting without change. The vitreous had quite cleared up, and there were several spots of choroidal atrophy. He was seen again December, 1903. The vision of the right eye was the same, and the same extensive choroidal changes (atrophy) were noted. The vision of the left eye was $\frac{2}{10}$.

The reporter remarks that although continuous use of the eyes on small objects is a recognized cause of inflammation of the eyeball, such results are rarely seen, the asthenopia accompanying excessive use usually causing the patient to desist before the danger-line has been crossed. It is also remarkable that the choroiditis came to an immediate standstill. It is interesting to note that the retina was unaffected, to any considerable degree, at least. It is also interesting to note that this was a traumatism rather than an infection, the former of which, with our present views upon infectious diseases, we are apt to ignore.

The Innervation of the Pupil.—PARSONS (*Roy. Lond. Ophth. Hosp. Rep.*, June, 1904) gives an exhaustive review and bibliography of a vast amount of research upon this subject, together with original experiments of his own. He sums up the results as follows: The iris contains a sphincter and dilator muscle, each of unstriped fibres. The sphincter is a compact ring of muscle near the pupillary margin. The dilator is a thin layer of muscle situated near the posterior surface, the constituent fibres being arranged radially. Each muscle has a separate and independent motor-nerve supply. Histological evidence alone has not succeeded in demonstrating beyond cavil the existence of a dilator muscle in the iris, but taken in conjunction with the physiological evidence it must now be considered proved. The histological difficulties are to be found in (1) the proof of the pres-

ence of radial muscle fibres other than those in the walls of the vessels, and in (2) the interpretation of the nature of the cells forming the posterior layers of the iris. These cells—*i. e.*, the anterior layer of retinal pigment epithelium—act as a dilator muscle. On bleaching and staining they resemble in all respects unstriped muscular fibres. Evidence also exists to show that the sphincter pupillæ is likewise derived from the retinal epiblast. These muscles would therefore resemble the arrectores pilorum of the skin in being formed from epiblast. The physiological evidence in favor of a distinct dilator is stronger than the histological, being indeed quite conclusive. The sphincter is innervated by the third cranial nerve, the pupil constrictor fibres originating in the third nucleus in the floor of the aqueduct of Sylvius, passing out of the mesencephalon in the third nerve as far as the orbit. The fibres here pass into the branch which supplies the inferior oblique, leaving it by the short root of the ciliary ganglion. From the ciliary ganglion they pass by the short ciliary nerves to the eye, piercing the sclera around the optic nerve, and thence forward in the choroid and ciliary body to the iris.

The dilator pupillæ are supplied by the cervical sympathetic nerve. The dilator tract probably commences in the neighborhood of the third nucleus in the mesencephalon, passing through the medulla oblongata, where its exact path is still unknown, into the lateral columns of the cord. The fibres leave the cord by the ventral routes of the first three thoracic nerves (cat, dog, ape), enter the rami communicantes, and run to the first thoracic or stellate ganglion. From here they mostly pass into the anterior limb of the annulus of Vieussens, though some run in the posterior limb. They pass up the neck in the cervical sympathetic to the superior cervical ganglion. From here the dilator tract enters the skull by the cervico-Gasserian strand, running independently of the carotid plexus. It joins the Gasserian ganglion and passes thence into the first or ophthalmic division of the fifth nerve, following the nasal branch, which it leaves finally to enter the long ciliary nerves, thus avoiding the ciliary ganglion. The long ciliary nerves enter the eye on each side of the optic nerve, and, running forward between the choroid and sclerotic, pass through the ciliary body to be distributed to the iris.

Constriction and dilatation of the iris are brought about respectively by three factors which are effectual in diminishing degree in the following order: Constriction—(1) contraction of the sphincter muscle; (2) relaxation of the dilator muscle; (3) dilatation of the bloodvessels. Dilatation—(1) contraction of the dilator muscle; (2) relaxation of the sphincter; (3) constriction of the bloodvessels.

Opaque Nerve Fibres.—HAWTHORNE (*The Ophthalmoscope*, September, 1904) figures two unusual instances of this condition. The first shows the extension of such fibres over an enormous area of the fundus, not only embracing the nerve in a complete circle about three disk diameters in extent, but also extending outward beyond the macula to a considerable distance, constituting in fact "by far the most conspicuous feature in the ophthalmoscopic picture." The disk itself, except for a small part of the lower and outer quadrant, was not involved. Another unusual feature was the absence of the lustrous appearance. The macular portion had, on the contrary, a dead-white character and

some irregularity of the surface. The eye appeared normal in other respects, but was totally blind without even perception of light, though it was not divergent and there was no nystagmus.

[Liebreich figures a very similar case in his atlas.—ED.]

In the author's second case an upward patch of about the usual size was completely separated from the disk by a clear interval of normal fundus, rather less than one-half disk diameter in width. This eye was healthy and had normal vision.

An Attempt to Estimate the Risk of Producing Sympathetic Ophthalmitis by Perforating Injury.—BARRETT, England (*Intercolonial Medical Journal of Australasia*, January 20, 1904), after reviewing briefly some well-known figures bearing upon sympathetic ophthalmitis, concludes that the "risk of sympathetic ophthalmitis supervening in a case of a severe injury with iridocyclitis is certainly not less than 5 per cent. It is probably considerably more." He feels, after attempting to assess the value of these facts, more inclined than ever to emphasize the rule gradually formulated in practice that in general, and apart from exceptional circumstances, a hopelessly blind eye, which has been perforated at any time, should be excised.

The Subconjunctival Injection of Cocaine in Cataract and Other Operations.—KOLLER, the discoverer of the anæsthetic properties of cocaine, remarks, in a paper read in the Section of Ophthalmology of the British Medical Association, which met at Oxford, July, 1904 (*The Ophthalmoscope*, September, 1904), that while cocaine was satisfactory in operations upon the superficial structures of the eyeball, it was disappointing in operations on the iris. To anæsthetize this membrane also, he practices, after a preliminary instillation of a mixture of cocaine and pilocarpine into the conjunctival sac, a subconjunctival injection —two to three drops—of a 5 per cent. solution at a point where the fixation forceps is to be applied. The injection must be subconjunctival, and not into the episclera, otherwise a troublesome œdema will occur which obscures the section.

A Case of Foreign Body Remaining in the Lens of the Eye for Six Years with the Lens Otherwise Clear.—LEWIS (*Medical Record*, August 6, 1904) reports a case of a young man whose lens has contained a foreign body for the past seven years, with retention of full vision and full functional activity of the eye. The foreign body entered the lens through a small wound at the lower nasal part of the cornea. It can be seen in the lens as a dark, glistening particle, a little to the supratemporal side and slightly posterior to the equator. It was thought to be a piece of steel, irregular in shape and about 2 mm. in its largest diameter, a chip from using a chisel on a piece of steel. There was almost no reaction and the wound healed promptly. There were two attacks of what seemed to be conjunctivitis during the four months following the injury. There were no further ocular symptoms, and the lens has remained clear.

OTOLOGY.

UNDER THE CHARGE OF

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Uræmia, with Deafness as a Complication.—DR. TREITEL (*Monatsschrift für Ohrenheilkunde*, November, 1903), in the following case, had an opportunity to observe both blindness and deafness occurring in the course of uræmia incident to scarlet fever in a child, and to have a differential diagnosis satisfactorily confirmed. The patient was taken ill with scarlet fever on October 12th. Fourteen days later an inflammation of the ear supervened. On November 7th albumin appeared in the urine; the child became delirious, with a high temperature and rapid pulse, and convulsions and vomiting followed. Upon November 10th, one month after the onset of the illness, the hearing was entirely wanting, and the possibility of labyrinth implication was considered, but set aside in favor of the conclusion that the aural symptoms were of uræmic origin. On November 15th the hearing reappeared, and on the following day the vision was restored.

The Question of the Value of Paracentesis of the Drum-head.—BUERKNER (*Archiv für Ohrenheilkunde*, August, 1904). In this paper the author, after citing authorities and defining the conditions under which paracentesis is presumably advisable in cases of acute suppurative inflammation of the middle ear, draws conclusions in favor of this procedure as contrasted with the occurrence of spontaneous opening, based upon his observations in 450 cases, in 300 of which he did paracentesis, the remaining 150 cases having come to him after the opening in the drum-head had been spontaneously established.

Of the paracentesis cases 76 per cent. were children and only 24 per cent. adults. The spontaneous perforations were more common in adults, 63.3 per cent. of these cases being children and 36.6 per cent. adults, the reason for this difference in the percentages in the two classes of cases being probably not so much the difference in the anatomical and pathological conditions as to the fact that in children the cases are brought to the notice of the surgeon at an earlier stage of the disease.

The proportion as to sex, in the paracentesis cases, namely, 6 to 4, was in accordance with the proportion of the sexes in all aural cases, 59.5 per cent. men and 40.5 per cent. women; while in the spontaneous perforation cases 55.4 per cent. were males and 44.6 per cent. females.

In an analysis of 200 paracenteses and 150 spontaneous perforation cases, of the former 172 healed within three days; there was recurrence of the inflammatory process in but 13 and mastoid complication in

but 1 per cent., while in the latter class 135 healed within three days; there were 26 cases of recurrence and 7.4 per cent. of mastoid complications.

The average duration of the inflammatory process, when paracentesis was done on the first day, was 7.6 days, when done on the second day 7.9 days, and when done later than the second day 8.6 days; where perforation occurred spontaneously on the first day the average duration was 17 days; on the second day the average was 24.7 days, and 26 per cent. of the spontaneous perforation cases became chronic.

In the paracentesis cases there was less subsequent disturbance of hearing than in the spontaneous cases, the proportion in the former being 3 per cent. and in the latter 12 per cent, the same advantage being shown for paracentesis in reference to the liability to recurrence of the disease, namely, but 8.5 per cent. in the former and 20.7 per cent. in the latter.

From these tabulated results of the observation of a limited number of cases, as well as upon the practical experience of over a quarter of a century, Buerkner concludes that in cases of otitis media with pain, swelling, or bulging of the reddened drum-head, and corresponding constitutional disturbances an early and free opening of the drum-head is the only rational procedure.

Contribution on the Surgical Cure of General Purulent Meningitis of Otitic Origin.—MARCEL LERMOYEZ and LEON BELLIN (*Annales des mal. de l'oreille, du larynx*, etc., tome XXX., No. 10) report two cases of purulent general meningitis of otitic origin cured by operation:

Case I. Female, aged nineteen years. For a year purulent discharge from the left ear, very abundant, fetid, at times tinged with blood, but without pain or disturbance of the general health. Later vague symptoms, headache, fatigue, and gastric disturbances. A few weeks later violent pains in the head, with vomiting. Signs of acute leptomeningitis, intense fronto-occipital headaches, pain on pressure upon the eyeballs. Slight left facial paralysis. Pupils equal, reacting to light. Fundus normal. Stiffness of the neck. Movements of flexion of the neck more difficult and painful than rotary movements. Patella reflex normal. Kernig's sign very marked.

Lumbar puncture: fluid transparent, under great pressure, containing lymphocytes, 58 per cent.; polynuclears, 40 per cent.; large mononuclears, 2 per cent.

Operation. 1. Mastoid opened at point of election: osteosclerosis of surface. Subcortical cells connecting with antrum filled with mucopus. 2. Opening of aditus and attic: middle ear filled with granulations, hammer carious, incus absent; facial nerve denuded at the level of the floor of the aditus to the extent of 5 mm. reddened, not œdematous, and could be raised from its canal. 3. Internal bony wall removed from level of roof of cavity, backward to the lateral sinus, which was intact without perisinal abscess. Dura thickened, covered with granulations, without perforation. A necrosed area of the inner wall of the middle ear without a fistula was apparent.

After operation the patient gradually improved. Lumbar puncture a week later showed: lymphocytes, 99 per cent.; polynuclears, 1 per cent.; fluid clear; headache was relieved; a fistula showed at the level of the aditus leading in the direction of the labyrinth. Another lumbar

puncture later showed a normal fluid. Two sequestræ were subsequently removed, the discharge ceased, the cavity epidermitized, and the patient was discharged well.

Case II. Otorrhœa from the right ear since infancy. Acute mastoiditis supervening, a petromastoid exenteration was performed. Eight days later there was acute general meningitis; the brain was then exposed and the exposure followed by incision of the dura mater and cerebral puncture. Four lumbar punctures were made within ten days; at each puncture ten to fifteen cubic centimetres of fluid were removed, which removal lessened the intense headaches and the stiffness of the neck. The pupils were unequal throughout the course of the disease.

Clinically, and by cytological examination of the cerebrospinal fluid, both of these cases were proven to be cases of purulent meningitis.

The writers conclude that the only complication of suppurative otitis which has baffled the surgeon, that is, purulent meningitis, may in the future be operated upon as successfully as the surgeon now operates in cases of brain abscess and sinus thrombosis. Four rules for the surgical treatment of purulent meningitis of otitic origin are then given, with detailed description.

Rule 1. Make a large opening of the middle ear and uncover the dura mater without going through it.

Rule 2. In case of failure of the preceding intervention, but in this case only, go through the dura mater in order to penetrate the subarachnoid space.

Rule 3. Practice and systematically repeat lumbar puncture.

Rule 4. Respect the labyrinth.

Practical Deductions from Our Recent Knowledge of Suppuration of the Labyrinth.—DUNDAS GRANT (*Annales des mal. de l'oreille, du larynx*, etc., tome XXX., No. 10) is of the opinion that many cases of suppuration of the labyrinth have no doubt been overlooked, because they have not been thought of or not looked for. It is a new surgical field; Jansen and Brieger have shown the frequence of labyrinthitis as a cause of otitic meningitis, and Jansen, Okada, and Whitehead have evidenced its frequency as a cause of cerebellar abscess. Jansen found labyrinthitis in from 20 per cent. to 25 per cent. of his cases of radical operation on the mastoid.

Prognosis. When the petromastoid exenteration alone has been done the mortality has been about 50 per cent., but with operation upon the labyrinth also the mortality has been reduced to 20 per cent.

Besides meningitis, cerebellar abscess is another important cause of death in labyrinthine suppurations (12 per cent. to 33 per cent.), and a practical deduction to be drawn is that in cases of cerebellar abscess a labyrinth lesion, and not always a lesion of the sinus, may serve to explain the cause of the abscess.

To prevent labyrinthine suppuration especial care in the treatment of middle-ear suppurations, acute as well as chronic, should be taken. The longer they have been without treatment, the greater the chance of labyrinthine affection, and careful note should be taken in the course of middle-ear suppuration of increase of deafness, of decreased osseous perception, of disturbances of equilibrium, or of positive vertigo, especially when associated with nystagmus, headache, and vomiting. During mastoid operations the external surface of the labyrinth

should be carefully examined for local signs of labyrinthitis, to which end it is necessary to use powerful electric illumination, and hydrogen peroxide or adrenalin to stop bleeding; as much as possible of the posterior bony wall of the auditory canal should be taken away, and a rotating burr preferably employed to diminish concussion, especially in removing the hard external wall of the attic. The gouges used should be sharp and always directed obliquely to the bone. In a small number of cases it is impossible to introduce Stacke's protector between the posterior auditory canal and the external semicircular canal.

Early Diagnosis. (*a*) Before operation study the disturbances of equilibrium, which are more marked when the head is turned toward the diseased side; also nystagmus, which often only exists when the eyes are turned toward the well side. Make hearing tests with great care, Weber's test being often misleading in cases of labyrinthine disease. (*b*) During the operation examine carefully the external semicircular canal, the oval window, the round window, and that part of the cochlea at the level of the promontory; remove completely the external wall of the attic and the "spur." (*c*) After mastoid operation labyrinthine suppuration is to be suspected if headache, fever, vertigo, vomiting, or nystagmus persist, or appear. Note the similarity between symptoms of labyrinthine suppuration and those of cerebellar abscess, the points of difference most marked being in cerebellar abscess, slow pulse and respiration, low temperature, tendency to coma and drowsiness, cerebral torpor, constipation, and wasting. Disturbances of equilibrium are rare in cerebellar abscess, but very constant in the acute stage of labyrinthitis. The gait in cerebellar affections is comparable to that of a drunken man, while in labyrinthitis there is more subjective feeling of vertigo and a gait which Moos compares to that of a duck. The two affections may coexist; in fact, in half the cases of cerebellar abscess there is suppurative labyrinthitis also. Suppurative labyrinthitis may be latent; cerebellar abscess may have a long latent period.

Indications for Operation. In general, if there is pus in the labyrinth; severe labyrinthine symptoms unaccounted for or unrelieved by mastoid operation; presence, or threatening, of symptoms of meningitis, cerebral abscess, cerebellar abscess or extradural abscess traceable to labyrinthine suppuration; if fistulæ and local signs of suppuration are found, in general if pus oozes, especially if it reappears after being wiped away.

Remarks. Evacuation of the labyrinth, unless necessary, adds to the risk of the operation. Suppuration is often limited to the external semicircular canal, a condition in which operation frequently leads to recovery. Inflammatory connective tissue in the internal auditory canal may prevent the suppuration from extending to the meninges. Nerve deafness may be due to a non-suppurative inflammatory lesion of the labyrinth. The openings of minute cells on the inner wall of the antrum should not be mistaken for fistulæ of the semicircular canal.

Operation. The best instrument, in the opinion of the author, is the rotating burr. Jansen, however, prefers the small chisels, 1½ to 3½ mm. in size. Sometimes it is impossible to avoid injuring the facial nerve. After opening the external semicircular canal the opening can be extended forward without difficulty into the vestibule. The burr may be used to enlarge the oval window inferiorly, and the cochlea may be opened with a very small burr in front of the round window.

PATHOLOGY AND BACTERIOLOGY.

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The Islands of Langerhans in the Normal and Diseased Pancreas of Man, and Especially in Diabetes Mellitus.—SAUERBECK (*Virch. Arch.*, 1904, Bd. 177, p. 1) contributes a critical review of the literature dealing with the changes in the islands of Langerhans in disease of the pancreas and in diabetes mellitus, together with an anatomical study of the organ in health and under various pathological conditions. He estimates that the normal pancreas contains from three to ten islands in an area of 3.7 cmm., the number varying a good deal in different parts of the organ. The islands in the interlobular form of chronic interstitial pancreatitis seem to be very resistant, while in lipomatosis of the pancreas without diabetes they may disappear to a considerable extent, though more frequently they are present in large numbers. The most remarkable resistance is seen in cases of carcinoma of the pancreas, in which condition they may remain entirely unaffected, even though considerable portions of the parenchyma are destroyed by the growth itself or by a secondary induration. In only 3 of 17 cases of diabetes mellitus was the pancreas extensively diseased. In eleven instances the organ showed either localized areas of sclerosis or a diffuse sclerosis of the interacinar type, lipomatosis, or other mild grades of alterations. In more than half the cases the islands presented some definite anatomical changes which were usually associated with disease of the parenchyma. The author, in summing up the results obtained by himself and by other observers, concludes that at least three organs must be kept in mind when considering the etiological possibilities of diabetes mellitus: the pancreas, liver, and nervous system. Experiments have demonstrated conclusively that complete removal of the pancreas is followed by glycosuria, while experiments and anatomical study have shown that provided the islands of Langerhans remain intact, practically the entire parenchyma of the organ may be destroyed without the occurrence of diabetes. Moreover, there has been no case of extensive disease of the islands reported without the presence of diabetes. If these facts speak for the "island theory" of diabetes mellitus, certain cases of suspected pancreatic diabetes that have been reported in which there was no disease of the islands seem to oppose it. In this latter group of cases the author believes that at least in some instances the diabetes may be dependent upon certain functional alterations of the islands not demonstrable with the microscope. He believes that in other instances the cause of the disease may be found in the liver or nervous system. He does

not consider that either functional or anatomical changes in the parenchyma of the organ are responsible for diabetes mellitus.

On the Formation of Uric Acid in Gout, and the Causes of Its Precipitation in the Tissues.—SCHMOLL (*Archiv. gén. de méd.*, 1904, t. ii. p. 2433), after discussing the formation of uric acid from nuclein, reviews the literature to show that neither the theory of retention nor the theory of increased production of uric acid in gout can be held to explain its presence in the serum of patients suffering from gout. The author rejects the theory of Roberts concerning the combination of sodium with the normal quadriurates in the blood, and advances the theory that under normal conditions the uric acid present is combined with thymic acid, the substance obtained when the xanthin bases are split off by oxidation from nucleinic acid. Thymic acid, then, is always present when uric acid is formed by oxidation. This method of formation Schmoll considers to be in operation during health. The combination of these acids cannot yet be detected. In gout, on the other hand, he considers the uric acid to be formed in part by synthetical processes, there being no production of thymic acid by this process. This absence accounts for the precipitable uric acid in the serum, which becomes deposited in the form of tophi. Two series of experiments in support of this hypothesis have been undertaken, the first to determine the influence of thymic acid on the excretion of uric acid, and the second to endeavor to obtain a proof of the synthetic formation of the uric acid in gout. In the first series it was found that administration of thymic acid to gouty patients greatly increased the amount of uric acid in the urine. This, the author considers, was due to the fact that the combination of uric and thymic acids takes place, and in this form the uric acid is much more readily passed into the urine. No such increase took place in normal individuals. The second series of experiments consisted in studying the constituents of the urine of a gouty patient under various diets. None of the changes of diet changed the amount of uric acid excreted in the urine, even though a diet free from nuclein bases was given. This the author considers can be explained only by assuming that uric acid is synthetically produced in the organism.

Experimental Streptococcus Arthritis in Relation to the Etiology of Acute Articular Rheumatism.—Although several English observers have recently done considerable work with the idea of isolating a specific organism pathogenic for rheumatic fever, their work has been done with very few or no control experiments.

R. I. COLE, in the *Journal of Infectious Diseases*, 1904, vol. i. p. 714, comments upon this fact and gives an account of his experiments with various strains of streptococci. The author obtained an organism from the blood of a patient during life, suffering from acute endocarditis which resembled culturally the ordinary streptococcus pyogenes, and which produced an arthritis in rabbits after intravenous injection. As the organism agreed quite closely with the so-called "micrococcus rheumaticus," Cole decided to use as control experiments streptococci isolated from various sources other than from patients with rheumatic fever. Six races of streptococci were used. These were obtained from peritonitis following carcinoma of the stomach; puerperal fever (autopsy);

blood during life in terminal septicæmia following myocarditis; empyema; blood during life in septicæmia following appendicitis; scarlet fever adenitis. The results of intravenous inoculation of these organisms into rabbits did not differ from those obtained in the experiments with the first organism from the case of acute endocarditis, nor did they differ in any marked degree from the experiments of those using the so-called "micrococcus" or "diplococcus" rheumaticus. Lameness was frequently produced, and, at autopsy, arthritis, from which lesions the organism could be regained, were frequently found. In 2 cases acute endocarditis was found at autopsy. One rabbit showed symptoms of inco-ordination similar to those that have been interpreted by other observers as chorea.

Cole concludes from these convincing experiments that arthritis and endocarditis may be produced by the intravenous inoculation of rabbits with streptococci from various sources, and the results obtained are quite similar to those described as resulting from the inoculation of the so-called "micrococcus" or "diplococcus" rheumaticus. He considers the description of a distinct variety or species of streptococci based upon the property of causing endocarditis and arthritis as unwarranted.

The Morphology of the Blood of Splenectomized Animals and of Animals with a Fistula of the Thoracic Duct.—CRESCENZI (*Lo Sperimentale*, 1904, Anno viii. p. 547) has studied the quantitative and qualitative changes in the white blood corpuscles of the dog after splenectomy combined with the formation of a fistulous opening from the thoracic duct. In most of the dogs the flow of lymph ceased after twenty-four hours on account of thrombosis of the duct; one dog lived for five days with patent duct. The appearance of the lymph varied with the periods of digestion, at this time being much more milky than when digestion was not taking place. The lymph contained from 3000 to 7000 white cells per cmm., practically all of which were small lymphocytes. Examination of the blood of normal dogs showed that both the total numbers of red and white cells as well as the relative proportions of white cells varied between rather wide limits. The following numbers show the maximum and minimum limits of variations: red blood corpuscles, 4,940,000 to 8,360,000; white blood cells, 7830 to 16,780; eosinophiles, 5.8 per cent. to 1.4 per cent.; polymorphonuclear 65.5 per cent. to 85.5 per cent.; large mononuclears, 0.2 per cent. to 1.7 per cent.; small mononuclears, 5.8 per cent. to 33.7 per cent.; transitional forms, 2.1 per cent. to 17.5 per cent.

The experiments are divided into four groups.

I. Simple exposure of the thoracic duct in cervical region.

II. Splenectomy followed by fistulous opening into the thoracic duct one to two days later.

III. Simple fistula of thoracic duct with free flow from central end.

IV. Splenectomy and fistula of thoracic duct at same operation.

Immediately after all these operations, including the control experiments, the blood showed an elevation of the polymorphonuclear leukocytes. This change was thought to be dependent upon the effects of the operation *per se*. The small mononuclear lymphocytes dropped in the control experiments within one to two hours after the operation to about one-third of their original number, but rose again within twenty-four hours to a height equal or above that seen before operation.

In the other three groups of experiments the drop was much greater and lasted longer. Often the decrease was to four-fifths and occasionally ten-elevenths of the original number, even twenty-seven hours after operation. If at the same operation splenectomy was performed and a fistula of the thoracic duct made, the effect was most pronounced. This phenomenon was not lasting, however, for these cells gradually rose to their original numbers as in the control experiments. The large mononuclear cells and transitional forms did not show any constant change. Occasionally they fell, often rose, and sometimes made their appearance in the circulating blood where before they had been absent. Owing to the extreme fluctuations of the numbers of these cells in the normal dogs, no definite conclusions could be drawn as to the effect which the operations might have upon them. The eosinophiles decreased regularly in both the control and experimental dogs, and sometimes disappeared entirely from the circulating blood. Quite as regular was their reappearance and gradual increase. The author concludes that when either a fistulous opening is made in the thoracic duct alone, or this operation is combined with splenectomy, the circulating blood shows a temporary decrease in the numbers of small lymphocytes. This diminution is slight but constant, and is dependent upon the loss of lymphocytes brought to the blood by way of the thoracic duct. The subsequent increase of lymphocytes and final establishment of the normal numbers is not dependent upon a vicarious function of the bone-marrow to form lymphocytes, since a histological study of the bone marrow showed no evidence of lymphocyte production. Indeed, no difference could be made out between the marrows of animals killed during the period of greatest lymphopœnia and the most marked lymphocytosis. Neither could any compensatory flow of lymph into the blood from channels other than the thoracic duct be discovered. Crescenzi therefore concludes that the small lymphocytes enter the circulation directly from the lymph glands. The experiments seem to show further that all the white cells do not arise from the same hæmopoietic organ, and that the large lymphocytes and transitional forms are not derived from the lymph glands.

Studies on the Pathological Anatomy of the Adrenals (Atrophy, Vicarious Hypertrophy, Tuberculosis).—Marakascheff (*Ziegler's Beiträge* 1904, Bd. xxxvi. p. 401), after studying the adrenal glands in cases of Addison's disease, and in certain conditions in which the glands were the seat of marked pathological change, concludes that the cortical substance is particularly involved in cases of Addison's disease, and destruction of this portion may be followed by the entire symptom-complex. Moreover, the medullary substance may be completely destroyed without the presence of Addison's disease. If one adrenal is destroyed, an hypertrophy of the cortex of the other one may take place; this hypertrophy leads to great compression of the medulla.

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